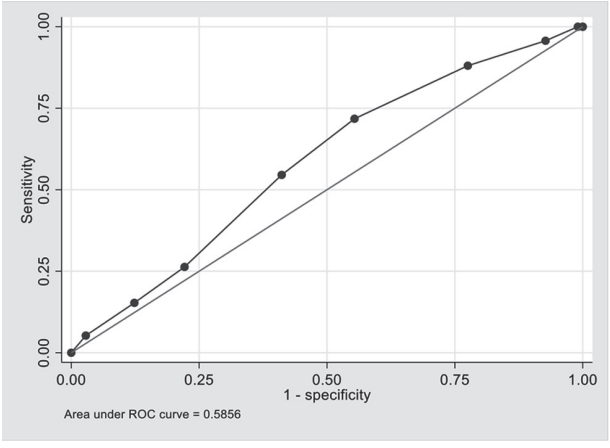
ETHIOPIAN JOURNAL OF REPRODUCTIVE HEALTH

EJRH

Visit us at www.ejrh.org

April, 2023 Volume 15, No. 2



www.esog-eth.org

Ethiopian Journal of Reproductive Health (EJRH)

April, 2023

www.esog-eth.org

www.ejrh.org

Ethiopian Society of Obstetricians and Gynecologists (ESOG)

Tel.: +251 115 506 068/069, Fax: +251 115 506 070
P.O. Box: 8731
Addis Ababa, Ethiopia
esogeth@gmail.com
newsletter@esog.org.et
www.esog-eth.org

Address:
Head Office:
Ras Desta Damtew Avenue
Tsehafi Tizaz Teferawork Keda Building (Near Ghion Hotel)
East Wing, 2nd Floor, Room no 7
ESOG Project Office:
Kirkos District/ Kazanchis
Nigist Towers, 3rd floor

Ethiopian Journal of Reproductive Health (EJRH)

April, 2023

Table of Contents PAGE

BIOCHEMICAL PREGNANCY OUTCOME AMONG DAY 3 VERSUS DAY 5 EMBRYO TRANSFER IN THE CENTER FOR FERTILITY AND REPRODUCTIVE MEDICINE AT A TERTIARY HOSPITAL IN ADDIS ABABA, ETHIOPIA

Mintesnot Mahtemsilassie, MD[1], Mekitie Wondafrash, PhD[2], Mustefa Negash, MD[1], Mesert Ansa, MD[1]

ABSTRACT

INTRODUCTION: The burden of infertility is the worst in sub-Saharan countries with the rare availability of assisted reproductive technology treatment. Even in areas where such treatment is available, low implantation and pregnancy rate is challenging health care providers which partially can be tackled by selecting the optimal day of embryo transfer. However, the effects of day of embryo transfer on pregnancy outcomes are an area of controversy even in countries with advanced fertility treatment.

OBJECTIVE: To see the effect of day of embryos transfer (day 3 vs. day 5) on biochemical pregnancy outcome in the center for fertility and reproductive medicine center at a tertiary hospital, Addis Ababa, Ethiopia.

METHOD: A retrospective record review conducted from January -December 2021 G.C.

RESULT: A total of 201 clients had undergone embryos transfer 107 were day 3 while 94 of them were day 5 embryos. Both groups are comparable in baseline characteristics like the mean age, the number and grade of embryo transferred. Biochemical pregnancy between day 3 and day 5 embryo transfer was similar in both groups 67 (62.6%) and 59 (62.8%) respectively (p=0.98).Although it is not statistically significant, the chance of having twin pregnancy was higher among day 5 embryo transfer (36%) compare to day 3 embryo transfer (17%) with p =0.053.

CONCLUSION: In women age less than 35, as long as good quality embryos available, transferring day 3 embryo is an alternative option over blastocyst transfer with comparable biochemical pregnancy without increasing the chance of multiple pregnancies.

KEY WORDS: day 5 and day 3 embryo transfer, Ethiopia, public fertility center, biochemical pregnancy

(The Ethiopian Journal of Reproductive Health; 2023; 15;1-8)

1 Department of Obstetrics and Gynecology, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
2 St. Paul Institute for Reproductive Health and Rights, Addis Ababa, Ethiopia

INTRODUCTION

Although infertility is a global problem, it is more common in low income countries, particularly in sub-Saharan Africa where it has significant burden on every aspect of an individual's life[1]. So taking this in to consideration World Health Organization (WHO) has declared "infertility as public health problem, alleviation of infertility therefore becomes a necessity on many levels"[2]. The most common cause of infertility in this part of the world is infection-related tubal damage which can be prevented and treated easily and effectively by assisted reproductive technology (ART), unfortunately this is rarely available. Even in areas where ART is available, it carries challenges to health care providers as evidenced by the low implantation and pregnancy rate(PR) which can be tackled partially by the day of embryo[1,3].
In most part of the world, embryos can be transferred back to the uterine cavity either on day 3 (D3) (cleavage stage) or day 5(D5) (blastocyst stages) after ovum pick up. However studies, regarding the effects of day of embryo transfer (ET) on fertility outcomes has shown varied results and most are with low quality[4,5]. On top of this a large meta-analysis revealed inconclusive result regarding the pregnancy outcomes comparing the two and recommended to have more studies on this controversial issue[6]. Having answers for this relevant intervention will also help providers to give more accurate counseling for couples as to the optimal day of transfer[4–7].

With the advancement of invitro culture one can extend duration of embryo in the lab to D5 and in theory this gives the opportunity to select genetically normal embryos. This allows transfer of few embryos and decrease chance of multiple gestation and its undue complications[3,4,8,9]. Transferring a blastocyst improves uterine/ embryonic synchronicity that could imitate the natural transfer of embryo from fallopian tube to endometrium[5,10].

However D5 transfer has its own drawbacks as there is an increased possibility of some of the embryos failing to develop to blastocyst in vitro resulting in cancellation of embryo transfer; and this again decreases number of embryos available for freezing and missing the opportunity of future transfer. There are technical difficulties in the cryopreservation/ thawing process in such expanded embryos. It is also associated with increased risk of monozygotic twining[5,8,9,11]. This study was conducted in a public in vitro fertilization (IVF) center where the embryology lab is busy, crowded with incubation to D5 embryos using single step culture media, unlike most settings where they use two steps media. This could have a different effect on pregnancy outcomes[3,12].

On the other hand, significant number of studies done on the success of IVF measured by implantation, pregnancy and live birth rates had shown transferring D3 embryo to be not inferior compared to D5 embryo transfers especially if the numbers of embryo available for transfer are fewer than three with comparable complications including multiple gestations. Performing D3 transfer in patients with few available embryos also reduces the incidence of cycle cancellation, therefore, associated with greater number of embryos available for freezing[5,7,8,11].

So the objectives of this study is to determine whether transferring D5 could result in better biochemical pregnancy than transferring D3 embryos . In addition, no local data are available regarding the effect of transfer day on biochemical pregnancy outcome. As this research was conducted in a public center having catchment of large population where patients are referred from different corners of the country with different socio-demographic characteristics, it could have a better representation of the situation regarding the outcome of pregnancy from day of embryo transfer and this is also important for generalization.

METHOD AND MATERIALS

Study setting, period, and design

It was conducted at Center for Fertility and Reproductive medicine (CFRM), department of Obstetrics and Gynecology, St. Paul's Hospital Millennium Medical College (SPHMMC), Addis Ababa, Ethiopia. The center, the first and only public IVF center for the country, is governed by the federal minster of health Ethiopia. Study was done though record review of patient cards and computer registers of clients who have visited the center from January to December 2021 G.C.

The study populations were all female partners age less than 35 years who have undergone IVF/ intra cytoplasm sperm injection (ICSI) cycles with fresh embryo transferred having at least one grade 1 embryo available for transfer. Couples with 1 or more failed IVF cycle were excluded. The outcome variable was biochemical pregnancy determined 2 weeks after embryos transfer. This is taken as positive if serum ß HCG greater than 25 mIU based on previous study cut off point values.

Ovarian stimulation protocol

In this fertility center three major stimulation protocol including long protocol, antagonist protocol, and minimal stimulation protocols are used. The first, a long protocol, was usually applicable for patients younger than 35 years with good ovarian reserve (AFC more than 5). The patients are appointed on day 21 of menses to get depot Goserelin(Zoladex) injection 3.6 mg subcutaneous stat after checking for cyst or dominant follicles, and then reappointed for stimulation either on second day of menses or 14 days from Zoladex injection whichever comes first. If no contraindication to start stimulation (no ovarian cysts >10 mm), stimulation started with calculated dose (based on age and BMI) with Human menopausal gonadotropin
(HMG) alone (Menopur) or in combination with recombinant FSH (Gonal-F) and the response followed with transvaginal ultrasound to see changes on the follicular size and endometrium and modification of doses made based on the response. Minimal stimulation protocol is applied for patient with poor ovarian reserve (AFC less 5), age more than 35 and who can't afford long protocol. With this protocol Letrozole 5mg PO is started on day 2 of the cycle and continued for 5 days and on the 4th day hMG SC 150 IU or 225 IU started . Once the leading follicle attained 14 mm in size, down-regulation with Cetrotide is instituted. Antagonist protocol is used rarely during the study period and usually used after failed minimal stimulation or for expected poor response. The only difference of antagonist from minimal stimulation protocol is that it is started directly with gonadotropin on second day rather than Letrozole and the doses of gonadotropin is not fixed and calculated based on age and BMI.

Triggering and ovum pick up (OPU)

Trigger for all three protocols is made with urinary HCG 10,000 IU or 5,000 IU SC, decided if 3 or more leading follicles reached 18 mm or more in size or greater or equal to 5 follicles reach/exceed 16mm in size. Ovum picks up procedure is done under transvaginal guidance after 36 h from HCG injection. The cycles either will be for IVF or ICSI depending on the semen analysis result. After OPU oral prophylactic antibiotic given and luteal support is started with injectable together with PO progesterone and estradiol valerate.

Fertilization and embryo transfer

Once the oocyte cumulus complex identified in the standard media it is kept in the incubator for 2 hours and decided for IVF or ICSI. Then embryos transferred back to the incubator. Patients called for embryo transfer by embryologist either on D3 or D5 after OPU is based on grade and number of embryo available. If the grade of embryo is grade 1 and more than 2 embryos available culture is extended to D5 without changing embryo culture media otherwise D3 embryos will be the final choice. If transfer is successful luteal support continue and patient appointed after 2 weeks to check for serum pregnancy test. If this is found to be positive, luteal support continued and appointed after 2 weeks for evaluation using Trans vaginal ultrasound (TVUS) and to check the presence of clinical pregnancy.

Ethical considerations

Ethical approval was obtained from the institutional review board of the researchers' institution (SPHMMC research ethical team). The information was extracted using structural questionaire with kobocollect toolbox without mentioning patient name. Confidentiality was maintained during data collection, analysis, and interpretation by avoiding recording of names and returning client records to their place after completion of data collection.

Data processing and statistical analysis

The data were checked for completeness and then imported into Stata statistical software release 15 (StataCorp, College Station, TX, USA) for analysis. Bivariate analysis were performed using proportions and means (standard deviation) for normal distribution, or medians (interquartile range) when the distribution was not normal. The association of the biochemical pregnancy result and independent variables were assessed using Fisher's exact test for categorical variables. Independent t-test, or the non-parametric test of difference of means (Mann Whitney U test) used for continuous variable. Statistical significance was declared at p=0.05 and all tests were two-sided. A full model assessing the relationship between the pregnancy test result and predictor variables was constructed after which non-significant variables were removed by a backward procedure using the likelihood ratio test (p<0.05).

RESULT

Table 1 -Baseline characteristics of patients who have undergone embryo transfers

Factor		D5(N=94)	D3(N=107)	p-value
Age of the woman in years, median (IQR)		29.0 (27.0, 32.0)	30.0 (28.0, 32.0)	0.27
Duration of infertility in years, median (IQR)		7.0 (4.0, 8.0)	6.0 (4.0, 9.0)	0.58
****Type of infertility**	Primary	65 (73.0%)	84 (81.6%)	0.16
	Secondary	24 (27.0%)	19 (18.4%)	
****Cause of infertility**	Female factor	48 (53.3%)	54 (52.4%)	0.96
	Male factor	23 (25.6%)	26 (25.2%)	
	Unexplained	6 (6.7%)	9 (8.7%)	
	Both	13 (14.4%)	14 (13.6%)	
****Hysterosalpingography result**	Not done	22 (25%)	22 (22%)	0.12
	Normal	16 (18%)	31 (31%)	
	Abnormal	50 (57%)	46 (46%)	
Total number of AFC (value), median (IQR)		17.0 (11.0, 22.0)	10.0 (6.0, 14.0)	<0.001

AFC =Antral follicular count

IQR = Interquartile range *P-value was calculated for categorical variable using Fisher exact test, for continuous variables The Mann-Whitney U (non-parametric independent t-test),IQR = Interquartile range ,**there are missing data during data collection

During the study period there were a total of 201 clients who had undergone embryo transfer fulfilling the inclusion criteria, 94 of them were D5 embryos and 107 were D3.The median ages were comparable between the two groups 29.0 (27.0, 32.0) and 30.0 (28.0, 32.0) respectively with P=0.27. They are also comparable in the type and cause of infertility. In both group primary type of infertility is common and accounted for 73.0 %(65) of day 5 and 81.6% (84) of D3 embryo transfers. Female cause of infertility is the common cause both in D3 and D5 embryo transfer 54 (52.4%) and 48 (53.3%) respectively. However, the median of total number of AFC is higher in D5 embryo transfer group (17.0 (11.0, 22.0)) comparing D3 embryo transfers group (10.0 (6.0, 14.0)) with p value <0.001 (Table 1)

Table 2 -Clinical data for D3 embryo transfer versus D5 transfer

Factor		D5 N=94	D3 N=107	p-value
Number of metaphase 2 oocytes (value), median (IQR)	Median	12.0 (9.0, 16.0)	5.0 (3.0, 8.0)	<0.001
Number of embryo developed available for transfer (value), median (IQR)	Median	6.5 (5.0, 7.0)	3.0 (2.0, 5.0)	<0.001
Number of embryo transferred(value), median (IQR)	Median	2.0 (2.0, 2.0)	2.0 (2.0, 2.0)	0.16
Method of sperm insemination for fertilization	IVF	43 (45.7%)	56 (52.3%)	0.35
	ICSI	51 (54.3%)	51 (47.7%)	
Level of physician who has transferred the embryo	Second-year Fellow	18 (19.1%)	15 (14.0%)	0.33
	Subspecialist	76 (80.9%)	92 (86.0%)	

*P-value was calculated for categorical variable using Fisher exact test, for continuous variables The Mann-Whitney U (non-parametric independent t-test),

In D5 embryo transfer group the median number of metaphase 2 oocytes and number of developed embryo available were 12.0 (9.0, 16.0), 6.5 (5.0, 7.0) respectively, all were significantly higher relative to D3 embryo transfer, 5.0 (3.0, 8.0), 3.0 (2.0, 5.0) respectively with p value in all cases<0.001. However in both groups the number of embryos transferred was two with at least one grade one embryo. Otherwise method of sperm insemination and level of physician doing the embryo transfer were comparable (Table 2).

Table 3 Predictors of biochemical pregnancy

Factors		Serum ß HCG		
		Negative (N=75)	Positive (N=126)	p-value*
Age cut at 30	<30 years	23 (30.7%)	65 (51.6%)	0.004
	>=30 years	52 (69.3%)	61 (48.4%)	
Duration of infertility in years, median (IQR)		7.0 (5.0, 10.0)	6.0 (4.0, 8.0)	0.007
Total number of AFC (value), median (IQR)		12.0 (6.0, 17.0)	13.0 (9.0, 21.0)	0.038
****Type of protocol used**	Long	33 (44.0%)	72 (57.6%)	0.13
	Minimal /mild	37 (49.3%)	49 (39.2%)	
	Antagonist	5 (6.7%)	4 (3.2%)	
Method of sperm insemination for fertilization	IVF	42 (56.0%)	57 (45.2%)	0.14
	ICSI	33 (44.0%)	69 (54.8%)	
Day of embryo transfer	D5	35 (46.7%)	59 (46.8%)	0.98
	D3	40 (53.3%)	67 (53.2%)	

*P-value was calculated for categorical variable using Fisher exact test, for continuous variables The Mann-Whitney U (non-parametric independent t-test), **there are missing data during data collection

Out of 201 patients 126 of them had positive serum ß HCG after 2 weeks of embryo transfer which accounted for 62.7 % of patients who have under gone embryo transfer who fulfill inclusion criteria. Looking at predictors of biochemical pregnancy age less than 30 significantly increase biochemical pregnancy compared to age greater than 30,65 (51.6%) and 61 (48.4%) respectively with p value = 0.004.Similarly a short duration of infertility with median of 6.0 (4.0, 8.0) has high chance of pregnancy relative to 7.0 (5.0, 10.0) together with this median of total number of AFC 13.0 (9.0, 21.0) has a better chance of biochemical pregnancy compare to 12.0 (6.0, 17.0) p=0.038.On the other hand type of protocol used, method of sperm insemination to oocyte and day of embryo transfer has no significant effect on the biochemical pregnancy (Table 3).

Table 4 Clinical outcomes for day 3 embryo transfer versus day 5 transfer.

Clinical outcome		D5 (N=94)	D3 (N=107)	p-value
Serum ß HCG positive	Yes	59 (62.8%)	67 (62.6%)	0.98
	No	35 (37.2%)	40 (37.4%)	
**Number of intrauterine pregnancies	Singleton	34 (64%)	48 (81%)	
	Twins	19 (36%)	10 (17%)	0.053
	Triplet	0 (0%)	1 (2%)	

*P-value was calculated for categorical variable using Fisher exact test, for continuous variables The Mann-Whitney U (non-parametric independent t-test), **there are missing data during data collection

Although the biochemical pregnancy between D3 and D5 embryo transfer was not statistically significant 67 (62.6%) and59 (62.8%) respectively p=0.98, the chance of having twins pregnancy was higher among D5 embryo transfer, 19 set of twin pregnancies (36%), compared to D3 embryo transfer 10 set of twins (17%) with p =0.053. there were 34 (64%) singlton pregnancies among D5 whereas 48 (81%) among day 3 embryo transfers. One triplet set of pregnancy was seen in D3 embryo transfers (Table 4).

DISCUSSION

To our knowledge this is the first type of study in Ethiopia to see the effect of day of embryo transfer on biochemical pregnancy. Although the comparison of the D5 vs D3 group was a retrospective and cross-sectional study, we believe that the two groups were closely matched. We selected 201 patients from both groups with age less than 35,having at least one good quality embryo (grade 1) and in both groups, 2(two) embryos have been transferred. Furthermore, the median age, duration of infertility, causes of infertility and type of infertility, the patients' parameters (SA, HSG results) and stimulation protocols all were comparable in both groups.

In this study although the number of oocytes retrieved ,number of mature oocytes and embryo available for transfer is significantly high in D5 relative to D3 ,the number of embryo transferred were equal(two) in both groups with similar quality of embryo. The chance of biochemical pregnancy was not significantly different in D5 embryo compared to D3, 59 (46.8%) and 67 (53.2%), respectively, with P=0.98.This result implied as long as we have good selection of patients in terms of age, quality of embryo and number of embryo transfer, the day of embryo transfer doesn't affect pregnancy outcome as it has been seen also in other studies[5–8,11].

The result of this study contradicted with the finding of other studies that demonstrate D5 embryos have a better pregnancy outcome[8,13–18].One of the attributing factors mentioned for the increased chance of pregnancy in D5 is the use of sequential culture which is believed to imitate the natural transfer of embryo from fallopian tube to the endomterium[13,14,16].However, in our study setting, the type of the culture media used is a one- step which might have partially contributed to the difference in the result of our study, as it has been seen in other parts of the world before the era of sequential culture media use, in which pregnancy outcome of D5 embryo was disappointing[11,17]. Prolongation of culture to day 5 may allow chromosomally competent embryos to develop to the blastocyst stage, thereby promoting intact embryos[16]. Despite the potential benefits of blastocyst-stage embryo transfer, it is not clear whether extension of embryo culture toward blastocyst production is a good option for all patients or all embryos in the same cohort[11].

The number of multiple significantly seen in this study was higher among D5 comparing to cleavage stage similar to the finding by Peter Schwarzler et al retrospective cohort study with increased risk of preterm delivery[16].However, in modern IVF practice it is encouraged to have single embryo transfer (SET) with singleton pregnancy to decrease the chance of having multiple pregnancy related complications[17]. So this study indirectly demonstrated that a day 5 embryo transfer predispose patients to multiple pregnancy that obviously will lead to increased risk of all complications of multiple pregnancy. A number of studies succeeded in decreasing chance of these complications by transferring single D5 embryo[14]. In view of the high incidence of multiple pregnancy in our study, in which all patient have received two blastocysts, we strongly recommend limiting the number of blastocysts transferred to one should be consider.

The limitations of this study are being retrospective study, and that it is only applicable in age group less than 35. The center is also using single step culture media for D5, unlike most settings where they use two step or sequential step for D5 culture, this might change the pregnancy outcome of D5 sage embryo. So in the future a prospective study involving all age groups after using D5 sequential culture media is recommended.

In conclusion, in women age less than 35 , as long as we have available good quality embryos, transferring day 3 embryo is an alternative option over blastocyst transfer with comparable biochemical pregnancy without increasing the chance of multiple pregnancies which in turn decreases the risk of complications related to multiple pregnancies. In addition, cleavage stage embryo transfer carries fewer burdens and cost in a set up with low resources and busy embryology labs. It has also less cost and stress for the patient.

CORRESPONDING AUTHOR:
Mintesnot Mahtemsilassie, MD
Department of Obstetrics and Gynecology, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
Email: mintmaht@gmail.com

REFERENCES

1. Sharma S, Mittal S, Aggarwal P. Management of infertility in low resource countries. BJOG. 2009 Oct;116 Suppl:77–83.
2. Infertility, WHO [Internet]. 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/infertility
3. Papanikolaou EG, D'haeseleer E, Verheyen G, Van de Velde H, Camus M, Van Steirteghem A, et al. Live birth rate is significantly higher after blastocyst transfer than after cleavage-stage embryo transfer when at least four embryos are available on day 3 of embryo culture. A randomized prospective study. Hum Reprod. 2005;20(11):3198–203.
4. Beesley R, Robinson R, Propst A, Arthur N, Retzloff M. Impact of day 3 or day 5 embryo transfer on pregnancy rates and multiple gestations. Fertil Steril [Internet]. 2009;91(5):1717–20. Available from: http://dx.doi.org/10.1016/j.fertnstert.2008.02.003
5. Glujovsky D, Farquhar C. Cleavage-stage or blastocyst transfer: what are the benefits and harms? Fertil Steril [Internet]. 2016;106(2):244–50. Available from: http://dx.doi.org/10.1016/j.fertnstert.2016.06.029
6. Blake DA, Proctor M, Johnson NP. The merits of blastocyst versus cleavage stage embryo transfer: A Cochrane review. Hum Reprod. 2004;19(4):795–807.
7. Utsunomiya T, Ito H, Nagaki M, Sato J. A prospective, randomized study: Day 3 versus hatching blastocyst stage. Hum Reprod. 2004;19(7):1598–603.
8. Coskun S, Hollanders J, Al-Hassan S, Al-Sufyan H, Al-Mayman H, Jaroudi K. Day 5 versus day 3 embryo transfer: A controlled randomized trial. Hum Reprod. 2000 Sep;15(9):1947–52.
9. Racowsky C, Jackson K V., Cekleniak NA, Fox JH, Hornstein MD, Ginsburg ES. The number of eight-cell embryos is a key determinant for selecting day 3 or day 5 transfer. Fertil Steril. 2000;73(3):558–64.
10. Fanchin R, Ayoubi JM, Righini C, Olivennes F, Schönauer LM, Frydman R. Uterine contractility decreases at the time of blastocyst transfers. Hum Reprod. 2001;16(6):1115–9.
11. Levron J, Shulman A, Bider D, Seidman D, Levin T, Dor J. A prospective randomized study comparing day 3 with blastocyst-stage embryo transfer [3]. Fertil Steril. 2002;77(6):1300–1.
12. Milki AA, Hinckley MD, Fisch JD, Dasig D, Behr B. Comparison of blastocyst transfer with day 3 embryo transfer in similar patient populations. Fertil Steril. 2000;73(1):126–9.
13. Gardner DK. Blastocyst culture: Toward single embryo transfers. Hum Fertil. 2000;3(4):229–37.
14. Karaki RZ, Samarraie SS, Younis NA, Lahloub TM, Ibrahim MH. Blastocyst culture and transfer: A step toward improved in vitro fertilization outcome. Fertil Steril. 2002;77(1):114–8.
15. Wu HX, Li KM, Ai L, Pan JP, Wang Y, Teng XM. The oocyte-to-baby rate of day 2, day 3 versus day 5 embryo transfer: A retrospective study. Clin Exp Obstet Gynecol. 2015;42(5):653–6.
16. Schwärzler P, Zech H, Auer M, Pfau K, Göbel G, Vanderzwalmen P, et al. Pregnancy outcome after blastocyst transfer as compared to early cleavage stage embryo transfer. Hum Reprod. 2004;19(9):2097–102.
17. Zech NH, Lejeune B, Puissant F, Vanderzwalmen S, Zech H, Vanderzwalmen P. Prospective evaluation of the optimal time for selecting a single embryo for transfer: day 3 versus day 5. Fertil Steril. 2007;88(1):244–6.
18. Scholtes MCW, Zeilmaker GH. A prospective, randomized study of embryo transfer results after 3 or 5 days of embryo culture in in vitro fertilization. Fertil Steril [Internet]. 1996;65(6):1245–8. Available from: http://dx.doi.org/10.1016/S0015-0282(16)58349-6

ASSOCIATION BETWEEN SERUM PROGESTERONE LEVELS AND ENDOMETRIAL STATUS ON HCG INJECTION DAY IN IVF CYCLE

Farideh Moramezi[1], Samaneh Ghobadi[1], Razeih Mohamad Jafari[1], Shabnam Salemi[1]*,

ABSTRACT

BACKGROUND: Endometrial thickness is a determining factor in successful implantation and pregnancy. So, this study is aimed at assessing the association between the serum levels of progesterone and endometrial status on the day of hCG injection in women treated with in-vitro fertilization.

METHODS: Totally, 71 women who underwent in-vitro fertilization cycle were prospectively recruited in this study. On the day of hCG injection, their serum progesterone levels were evaluated with the ELISA kit. The endometrial thickness was examined using transvaginal ultrasound. Patients were divided into two groups, including patients with progesterone level ≤ 1 ng/ml and those with progesterone level > 1 ng/ml. Eventually, patients' demographic and clinical features were statistically compared between two groups.

RESULTS: Among all the evaluated factors, the rate of gravidity in patients with progesterone level ≤ 1 ng/ml was significantly lower than those with progesterone level > 1 ng/ml (P=0.02). But the rate of abortion in patients with progesterone level ≤ 1 ng/ml was significantly higher than another group (P=0.02). Moreover, the mean endometrial thickness was not significantly different between the two groups (P= 0.83).

CONCLUSION: The progesterone levels on the day of hCG injection had no significant effect on the endometrial thickness. Nevertheless, a strong negative correlation between the progesterone levels and the abortion rate implies that the progesterone may probably affect the IVF clinical outcomes in a way other than changing the endometrial thickness.

KEYWORDS: Progesterone, Endometrial thickness, Human chorionic gonadotropin, In-vitro fertilization

(The Ethiopian Journal of Reproductive Health; 2023; 15;9-15)

1 Department of Obstetrics and Gynecology, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

INTRODUCTION

The human endometrium is a unique, elastic, dynamic, steroid-sensitive tissue that undergoes periodic changes during the menstrual cycle, including proliferation, differentiation, destruction, and repair[1]. These changes are regulated by estrogen and progesterone hormones to allow implantation during the relatively short "implantation window" period of the menstrual cycle. In fact, the physiological functions of the endometrium is to allow blastocyst replacement and support the pregnancy after the implantation[1,2]. Therefore, endometrial receptivity is essential for successful implantation, both in normal pregnancy cycles and in vitro fertilization (IVF) cycles[3].

Discovering the relationship between biological and hormonal markers with the clinical outcomes in various diseases increases our understanding of pathophysiology and the exact mechanism behind those clinical outcomes[4]. Several factors can affect endometrial receptivity, and endometrial thickness is one of the parameters that can be used as an indirect indicator of its acceptability[5,6]. During the normal ovulation cycle, a female sex hormone called progesterone is released from the corpus luteum, which its interruption causes menstruation through expelling the extra layer of the uterus. In addition, this hormone is released during pregnancy. Progesterone is used in medical strategies such as contraception, abortion, amenorrhea treatment, hormone therapy in postmenopausal women[7]. Also, immediately after oocyte implantation, human chorionic gonadotropin (hCG) hormone is produced by the placenta, which is essential for maintaining pregnancy. During the first weeks of pregnancy, hCG causes more natural progesterone to be produced, which ultimately leads to menopause[8].

Injections of hCG for pregnancy play a major role in the treatment of infertility in both men and women. This polypeptide hormone plays a vital role in the normal growth of oocytes in a woman's ovaries[9]. Moreover, only 30 to 35% of assisted reproductive techniques (ART) cycles are successful to treat infertility while infertile couples expect a high probability of success with high financial and time costs. Therefore, in ART cycles such as IVF, intracytoplasmic sperm injection (ICSI), ovarian stimulating hormones are used[10]. In this regard, progesterone plays an important role in preparing the endometrium for embryo implantation and successful pregnancy in ART-related cycles. Therefore, this study was performed to determine the relationship between the serum levels of progesterone and endometrial status on the day of hCG injection in the IVF cycle.

MATERIAL AND METHODS

Study Design and Population

This prospective study was performed on infertile women treated with IVF in the infertility ward of Imam Khomeini Hospital. This research was approved by Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran with Ethical Code: IR.AJUMS.HGOLESTAN.REC.1399.132, and all participants signed the informed consent prior to enrollment. All proceedings and documentation were overseen by local institutional ethics committee of hospital center.

All volunteer patients treated with IVF were recruited in the study. But those with adenomyosis, myoma, and patients undergoing GnRH agonist triggering or hCG triggering were excluded from the study.

Procedure

All couples referred to in the infertility ward of Imam Khomeini Hospital between 2020-2021 were invited to this study, and received the consent form after informing about the study procedure. Women, who voluntary agreed to participate and signed their consent form, received a baseline questionnaire form. A clinic nurse along with an investigator visited and followed up the patients during the treatment period until the end of the study, and collected their data. A physician added the medical details related to ART procedure and results of laboratory tests.

Based on the serum levels of progesterone on the day of hCG injection, patients were categorized into two groups, including patients with the progesterone level ≤ 1 ng/ml and those with the progesterone level > 1 ng/ml. All demographic and clinical features [e.g., gravity, parity, the number of cesarean sections, the number of natural deliveries, the history and number of abortions, cause and type of infertility, duration of infertility, the number of IVF failures] were statistically assessed and compared between the two groups.

Measurements

To separate serum, 2cc of intravenous blood was taken from all patients on the day of HCG injection and all serum samples were kept at minus 20°C until the end of sampling time. At the end of the sampling time, the progesterone level of the samples was measured with a sensitivity of 0.1ng/ml with the ELISA kit in the Dr. Mostofi's laboratory. Also, the condition of the endometrium, including the appearance and the thickness of the endometrium were evaluated by transvaginal ultrasound.

Statistical Analysis

To describe the data, the mean and standard deviation for quantitative variables and frequency and percentage for qualitative variables were used. Data were analyzed using a t-test (Mann-Whitney test if necessary), and Chi-square test when appropriate. $P < 0.05$ is considered as statistically significant. All analyzes were done using statistical software SPSS version 26.0 (IBM Corporation, Armonk, NY).

RESULTS

In this study, 71 patients in age ranging from 25 to 44 years (35.05 ± 5.10) with a history of infertility and IVF were evaluated. As shown in Table 1, all patients were evaluated for demographic and clinical information. Most patients have been treated with IVF at least once but this treatment process has failed for them. Overall, the mean serum progesterone level and endometrial thickness on the day of hCG injection were 1.44 ± 1.97 ng/ml and 8.99 ± 1.89 mm, respectively (Table 1). Also, the most prevalent causes of infertility in patients were male factors (53.5%), female factors (32.4%), male and female factors (9.9 %), and unexplained causes (4.2%), respectively.

Table 1. Description of demographic information, clinical manifestations in the studied patients.

Variables	Mean ±SD	Frequency (%)
Age	35.05 ± 5.10	-
weight	71.62 ± 9.69	-
height	164.72 ± 7.40	-
BMI	27.03 ± 3.96	-
Gravidity		
Nulligravid	_	29 (40.8)
		42 (59.2)
Parity		
Nulliparous	_	9 (12.7)
		62 (87.3)
Number of natural deliveries	_	1 (1.4)
Number of cesareans	_	8 (11.3)
Abortion	_	24 (33.8)
Infertility period (years)	5.63 ± 3.90	-
Number of IVF failures	_	62 (87.3)
Serum progesterone levels	1.44 ± 1.97	-
Endometrial thickness	8.99 ± 1.89	-
Type of abortion		
Spontaneous	-	18 (25.4%)
Curettage	-	5 (7%)
Right salpingectomy	-	1 (1.4%)
Type of infertility		
Primitive	-	39 (54.9%)
Secondary	-	30 (42.3%)
Primitive/secondary	-	2 (2.8%)
Cause of infertility		
Male & Female factors	-	7 (9.9 %)
Unexplained factor	-	3 (4.2%)
Male factor	-	38 (53.5%)
Female factor		23 (32.4%)

Comparison of demographic and clinical features between two groups

As illustrated in Table 2, there was no significant difference between the two groups in terms of age, body mass index (BMI), parity, live child birth,

number of natural deliveries, number of cesarean sections, type of abortion, infertility period (years), and number of IVF failures (P >0.05). Among all the evaluated factors, the rate of gravidity in patients with the progesterone level ≤ 1 ng/ml was significantly lower than those with progesterone level > 1 ng/ml (P=0.02). But the rate of abortion in patients with the progesterone level ≤ 1 ng/ml was significantly higher than those with progesterone level > 1 ng/ml (P=0.02). Also, the rate of parity in cases with the progesterone level > 1 ng/ml was higher than those with progesterone level ≤ 1 ng/ml, but not significantly so (P= 0.13).

The number of pregnancies is defined as gravidity. Parity refers to the number of times a woman with a gestational age of 24 weeks or more gives birth to a fetus, regardless of whether the baby is alive or dead.

Comparison of endometrial thickness between two groups

As shown in Table 2, the mean (SD) endometrial thickness was not significantly different between the two groups (P= 0.83).

Table 2. Comparison of studied factors between the two groups

Variables	Progesterone levels ≤ 1 N=48	Progesterone levels > 1 N=23	p. value
Age	34.65 ± 5.34	35.67 ± 4.74	0.41
weight	73.71 ± 10.55	68.47 ± 7.34	0.09
height	164.90 ± 8.01	164.46 ± 6.54	0.81
BMI	27.93 ± 4.37	25.65 ± 2.76	0.09
Endometrial thickness (mm)	9.03 ± 1.2	8.93 ± 2.6	0.83
Nulligravid	33 (68.7)	9 (39)	0.02*
Gravidity	15 (31.3)	14 (61)	
Parity	4 (8.4)	5 (21.7)	0.13
Nulliparous	44 (91.6)	18 (78.3)	
Live child birth	3 (6.2)	5 (21.7)	0.1
Stillborn	1 (2.1)	0	1
Number of natural deliveries	0	1 (4.3)	0.32
Number of cesarean sections	3 (6.2)	5 (21.7)	0.1
Abortion	21 (43.7)	3 (13)	0.02*
Length of infertility (years)	5.10 ± 3.72	6.44 ± 4.09	0.15
Number of IVF failures	45 (93.8)	18 (78.3)	0.1
Type of abortion			
Spontaneous	14 (29.1%)	3 (13%)	0.5
Curettage	5 (10.4%)	0 (0%)	
Right salpingectomy	2 (4.1%)	0 (0%)	
Type of infertility			
Primitive	25 (52.1%)	17 (73.9%)	0.2
Secondary	21 (43.7%)	5 (21.7%)	
Primitive/secondary	2 (4.1%)	1 (4.3)	
Cause of infertility			
Male & Female	6 (12.5%)	1 (4.3%)	0.5
Unexplained	2 (4.1%)	1 (4.3%)	
Male Factor	23 (47.9%)	15 (65.2%)	
Female Factor	17 (35.5%)	6 (26.2%)	

DISCUSSION

In the present study, the most common causes of infertility in both groups were respectively male and or female factors. No significant association was found between the serum progesterone levels on the day of hCG injection and demographics (age and BMI) and most clinical features, including the rates of live child birth, stillborn, natural deliveries, cesarean sections, length of infertility, history of IVF failures, and types of abortion and infertility, and causes of infertility. By contrast, Whynott et al. reported a significant negative correlation between the serum progesterone level after a cryopreserved embryo transfer cycle and both BMI and weight in patients undergoing IVF; approximately 30% of patients with body weight ≥ 90.7 had serum progesterone levels <15 ng/mL. However, no significant effect of the progesterone levels on live birth rate was found[11], which was in agreement with the corresponding result in the present study.

The serum progesterone level was significantly associated with gravidity and abortion. But, no significant effect of the progesterone level on the day of hCG injection on the endometrial thickness was detected in women treated with IVF. These findings confirm the results of the previous studies[12,13] that reported a positive correlation between the endometrial thickness and the successful process of implantation and pregnancy, but a negative relationship with abortion.

Previous studies demonstrated that low luteal progesterone levels had a significant adverse effect on ongoing pregnancy and live birth rates in patients undergoing ART procedures[14]. In the present study, although the progesterone levels were significantly associated with gravidity and abortion, the rates of stillborn and live child birth seem not to be significantly affected by the progesterone levels. This contradictory result may be due to the insufficient sample size, which demands further investigations in larger population.

The findings of Davar et al.'s study showed no relation between the endometrial thickness and the serum levels of estradiol and progesterone at 5 to 7 days after ovulation. However, a significant correlation was observed between the endometrial thickness and estradiol serum level only in the age group of <20 years[15]. On the other hand, several studies have reported conflicting results about endometrial thickness changes during IVF cycle[16]. Bu et al. assessed the endometrial thickness change in response to progesterone injection and found that the endometrial thickness increased or remained constant after progesterone injection. Also, Bu et al. reported that an increase in endometrial thickness after progesterone injection was associated with better pregnancy outcomes[16]. Contrary to the results of Bu et al.'s study, Haas et al. reported that endometrial thickness may become thinner after progesterone administration[17]. In this regard, Kim et al. reported that progesterone levels at 14 days after oocyte retrieval could be a good indicator of pregnancy during infertility treatment[18]. Such conflicting results in different studies may be affected by differences in the sample size and/or type or methodology of the study, which requires more precise investigations.

CONCLUSION

Results of the present study proposed that the serum level of progesterone on the day of hCG injection had no significant effect on the endometrial thickness. However, a strong negative correlation was detected between the serum progesterone levels and the abortion rate, implies that the progesterone may probably affect the IVF clinical outcomes in a way other than changing the endometrial thickness. Considering the challenging role of progesterone in changing the endometrial thickness and IVF outcomes, clinical trials on more diverse populations are required to obtain definite results.

ACRONYMS:

IVF: in vitro fertilization
hCG: human chorionic gonadotropin
ART: assisted reproductive techniques
ICSI: Intracytoplasmic sperm injection
BMI: body mass index

CORRESPONDING AUTHOR:
Samaneh Ghobadi
Obstetrics-Gynecology Residence at Department of Bbstetrics and Gynecology, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
Email address: samaneh.ghobadi2@ajums.ac.ir

REFERENCES

1. Salamonsen L.A. Menstrual Fluid Factors Mediate Endometrial Repair. Front. Reprod. Health 2021;3: 779979.
2. Massimiani M., Lacconi V., La Civita F., Ticconi C., Rago R., & Campagnolo L. Molecular Signaling Regulating Endometrium-Blastocyst Crosstalk. Int J Mol Sci. 2019;21(1):23.
3. An J, Li L, Zhang X, Liu L, Wang L, Zhang X. A clinical and basic study of optimal endometrial preparation protocols for patients with infertility undergoing frozen-thawed embryo transfer. Exp Ther Med. 2020;20(3):2191-2199.
4. Hosseinzadeh M., Pouladzadeh M., Eftekhar A., Choghakabodi P. M., & Sokooti, A. Evaluation of D-dimer as a predictor of severity, degree of pulmonary involvement and mortality in patients with COVID-19. Scientia Medica. 2022;32(1):e43281.
5. Bai X, Zheng L, Li D, Xu Y. Research progress of endometrial receptivity in patients with polycystic ovary syndrome: a systematic review. Reprod Biol Endocrinol. 2021;19(1):122.
6. Zargar M, Pazhouhanfar R, Najafian M, Choghakabodi P.M. Effects of intrauterine autologous platelet-rich plasma infusions on outcomes in women with repetitive in vitro fertilization failures: a prospective randomized study. Clin. Exp. Obstet. Gynecol. 2021; 48(1):179–184.
7. Vikas S, Swati G. The impact of progesterone level on day of hCG injection in IVF cycles on clinical pregnancy rate. J Hum Reprod Sci. 2017;10(4):265.
8. Oliveira R, Cabral FG, Carvalho WAP, Cordts EB, Bianco B, Barbosa CP. Progesterone level on the day of hCG administration in relation to the pregnancy rates of patients undergoing assisted reproduction techniques. Einstein (Sao Paulo). 2017;15(3):273-277.
9. Mehrafza M, Raoufi A, Rahimian T, Nikpouri Z, Nasrollahzadeh M, Abdollahian P, et al. Evaluation of the role of serum progesterone level on the day of human chorionic gonadotropin administration on intracytoplasmic sperm injection outcome. pajoohande. 2014;19(4):184-188.
10. Zargar M, Dehdashti S, Najafian M, Choghakabodi PM. Pregnancy outcomes following in vitro fertilization using fresh or frozen embryo transfer. JBRA Assist Reprod. 2021;25(4):570-574.
11. Whynott RM, Summers KM, Jakubiak M, Van Voorhis BJ, Mejia RB. The effect of weight and body mass index on serum progesterone values and live birth rate in cryopreserved in vitro fertilization cycles. F S Rep. 2021;2(2):195-200.
12. Chen SL, Wu FR, Luo C, Chen X, Shi XY, Zheng HY, et al. Combined analysis of endometrial thickness and pattern in predicting outcome of in vitro fertilization and embryo transfer: a retrospective cohort study. Reprod Biol Endocrinol. 2010;8:30.
13. Zhao J, Zhang Q, Li Y. The effect of endometrial thickness and pattern measured by ultrasonography on pregnancy outcomes during IVF-ET cycles. Reprod Biol Endocrinol. 2012;10:100.
14. Ranisavljevic N, Huberlant S, Montagut M, Alonzo PM, Darné B, Languille S, et al. Low Luteal Serum Progesterone Levels Are Associated With Lower Ongoing Pregnancy and Live Birth Rates in ART: Systematic Review and Meta-Analyses. Front Endocrinol (Lausanne). 2022;13:892753.
15. Davar R, Dehghani Firouzabadi R, Chaman-Ara K. Relation between endometrial thickness with serum estradiol and progesterone levels in patients visited at Ob&Gyn clinic of Shahid Sadoughi hospital. Iran South Med J. 2015;17(6):1213-1222.
16. Bu Z, Yang X, Song L, Kang B, Sun Y. The impact of endometrial thickness change after progesterone administration on pregnancy outcome in patients transferred with single frozen-thawed blastocyst. Reprod Biol Endocrinol. 2019;17(1):99.
17. Haas J, Smith R, Zilberberg E, Nayot D, Meriano J, Barzilay E, et al. Endometrial compaction (decreased thickness) in response to progesterone results in optimal pregnancy outcome in frozen-thawed embryo transfers. Fertil Steril. 2019;112(3):503–9.e1.
18. Kim YJ, Shin JH, Hur JY, Kim H, Ku S-Y, Suh CS. Predictive value of serum progesterone level on β-hCG check day in women with previous repeated miscarriages after in vitro fertilization. PLoS ONE. 2017;12(7):e0181229.

RELATIONSHIP BETWEEN ENDOMETRIAL THICKNESS AND PREGNANCY OUTCOMES IN ASSISTED REPRODUCTIVE TECHNOLOGY CYCLES

Mutasim Abdullahi, MD, MPH[1]

ABSTRACT

OBJECTIVE: To explore the relations of different ultrasonic endometrial thickness (EMT)values on hCG trigger day and the pregnancy rate (PR) after fresh embryo transfer (ET) in controlled ovarian stimulation (COS) cycles.

BACKGROUND: Successful implantation and delivery require both the functional embryo and receptive endometrium in assisted reproductive technology (ART) cycles which is an expensive procedure with low implantation and pregnancy rate (PR). It is estimated that embryos account for one-third, and suboptimal endometrial receptivity for the remaining two-thirds of implantation failures. There is still an ongoing debate regarding the predictive ability of ultrasonic endometrial evaluation on the day of human chorionic gonadotrophin (hCG) trigger during controlled ovarian stimulation (COS) on the outcomes of pregnancies after in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI).

METHOD: A retrospective review of data from medical records of all patients who underwent COS, oocyte retrieval, IVF/ICSI, and fresh ET between March 2021and July 2022 at Centre for Fertility and Reproductive Medicine (CFRM), St Paul Millennium medical College (SPHMMC) Addis Ababa, Ethiopia. Patients were categorized based on their ET outcome (as pregnant or non-pregnant) and EMT values on the day hCG trigger (groups A <8mm, B 8-12mm, and C>12 in mm) to study and analyze if any relation between endometrial thickness and pregnancy rate existed.

RESULTS: A total of 548 records were analyzed. PR was 40.9%. The odds of pregnancy were higher among patients with EMT group B (82.8% vs 74.6%, p=0.05) and was shown to be significant after controlling for the effects of multiple confounding factors. Although receiver operator curve (ROC) analysis indicated that EMT has a limited value to be used as an indicator of the pregnancy rate as evidenced by the area under the curve (AUC) of 0.59 (95% CI= 0.53, 0.63), it was not possible to determine a cutoff of the endometrial thickness value with an acceptable trade-off between sensitivity and specificity

CONCLUSION: There is a positive relationship between the EMT measured on the day of hCG injection and PR and that EMT is an independent factor. Further prospective study is needed to explore the issue in more detail in our setup.

KEY WORDS: assisted reproductive technology, controlled ovarian stimulation, in vitro fertilization, intracytoplasmic sperm injection, endometrial thickness, embryo transfer

(The Ethiopian Journal of Reproductive Health; 2023; 15;16-24)

1 CFRM, SPHMMC, Addis Ababa Ethiopia

INTRODUCTION

It is estimated that embryos account for one-third, and suboptimal endometrial receptivity for the remaining two-thirds of implantation failures in Assisted reproductive treatment (ART) cycle which is an expensive procedure with low implantation and pregnancy rate. Successful implantation and delivery require both the functional embryo and receptive endometrium in assisted reproductive technology (ART) cycles.

A 2D grayscale ultrasound EMT measurement during monitoring in ovarian stimulation in IVF cycles can be an indirect marker of endometrial receptivity (ER) at low resource settings as in our setup[1,2].

Ultrasonographic endometrial thickness ranges from 1 to 4mm in the menstrual phase, 4 to 8mm in the mid-proliferative phase, 8 to 14mm in the late follicular phase, and 7 to 14mm in the secretory phase.

Studies on the potential relationship between ultrasonic EMT on the day of hCG administration and IVF/ICSI ET pregnancy outcome came up with mixed results. While several studies have suggested a positive correlation[2,3], other multiple studies have refuted the correlation, Shakerian and suggest that neither individual nor combined analysis of EMT and pattern had predicting effects on live birth following IVF treatments, and embryo quality might be the one that really has effects[4,5].

While some studies demonstrated a higher pregnancy rate at certain endometrial thickness 11,50. no conclusive cut-off value of endometrial thickness has been established in order to help ART providers in counseling the couple about the outcome.

The aim of this study is to examine the relationship between endometrial thickness measured on the day of administration of human Chorionic Gonadotrophin (hCG) on pregnancy rate and if possible, to identify a cut off value at which pregnancy rate is too low.

METHOD

Study setting, design, and period

The study was a retrospective cross-sectional study in which clinical data of all fresh IVF/ICSI cycles performed between March, 2021 to July 2022 at CFRM - SPHMMC, Addis Ababa, Ethiopia was reviewed. The study included all first fresh ETs cycles in women aged 18–45 years. Exclusion criteria used were incomplete record (missing values), frozen embryo transfer cycles, abnormal uterine cavity as demonstrated by HSG, SHG or hysteroscopy, and previous failed IVF/ICSI ET cycle. Our center is rendering comprehensive ART services except donor gametes, perinatal genetic diagnosis, and surrogacy. Three major stimulation protocol used in our center are the conventional long agonist, antagonist, and minimal protocols. The choice of COS protocol, the starting dose of gonadotropin and monitoring frequency were based on the institution's standard protocol. Endometrial thickness was measured in the midsagittal plane of the uterus as the maximum distance between the 2 interfaces of endometrial–myometrial junction. Patients were assigned on hCG administration day into either of three groups depending on the endometrial thickness; groups A: <8mm; B: 8-12mm. C: >12mm.ovulation was triggered using a 5,000 -10,000 IU SC urinary HCG or decapeptyl when indicated. Thirty-six hours later ultrasound guided oocyte retrieval procedure using a single lumen 17G, 35cm long aspiration needle under light anesthesia will be performed. Partners' semen will also be collected the same day for subsequent IVF/ICSI use. Luteal support was initiated on the same day after oocyte retrieval procedure with for all and continued in the event of positive serum hCG until 12th week. After IVF/ICSI- procedures were carried out as per indication the derived embryos were classified according to the Istanbul consensus 11. A fresh maximum of 2–3 cleavage-stage embryos (day 3) or 1-2 day 5 embryos were transferred accordingly. Serum hCG levels were assessed two weeks after oocyte retrieval and ultrasound scan confirmation of all pregnancies was performed on all patients between five to six weeks estimated gestational age based on ET day.

Data Compilation and Statistical Analysis

Data were compiled and entered initially using excel 2022 and shipped to Stata 11 software for coding, cleaning, and analysis. All tests were two tailed, and $p < 0.05$ was considered statistically significant. Continuous variables were presented as mean and SD and were tested by student's t-test. Comparisons of proportions were made by the chi squared test. The effect of endometrial thickness on the pregnancy outcome was studied using multivariate analysis, where all other factors affecting the pregnancy outcome were controlled for. To determine the independent relation of endometrial thickness and pregnancy rate a stepwise logistic regression analysis was performed using aforementioned confounding factors in the Stata software. The Receiver operating characteristic (ROC) analysis was used to evaluate if an endometrial thickness can predict pregnancy outcome.

RESULTS

Out of the total 1286 embryo transfers performed during the 15 months of the study period, only 548 cycles were eligible for inclusion in the study. Most of the exclusions were due to incomplete and missing data. Total, biochemical, and clinical pregnancy rates were 40.9%, 36.2% and 4.7% respectively. Spontaneous abortion rate was 1 %. Endometrial thickness measured on the day of hCG administration ranged from 5 to 14 mm.

Almost four fifth of the women were aged younger than 35 and had more than five AFCs at the start of the stimulation. Majority of the patients had no adnexal or uterine pathology (89% and 93.7% respectively), had normal semen analysis result (85%), or had a history of previous pregnancy by the male partner (84.2%), had grade B (77.9%) and trilaminar endometrium (99.1%) on the day of hCG administration, oocyte retrieval of more than five (76.9%) and their embryo transfers were performed by REI subspecialists (88.5%). ICSI was performed more often (53.4%) than IVF. Minimal stimulation protocol (52.8%) was the most often used method (Table 1).

Table 1: Characteristics of women who underwent IVF/ICSI fresh ET procedures in the study

Characteristics	No.	%
Age of the woman		
<35 y	298.0	78.6
>=35 y	81.0	21.4
AFC		
>=5	435.0	80.6
<5	105.0	19.4
Duration of infertility		
<5 y	256.0	48.3
≥5 y	274.0	51.7
Adnexal pathology		
Absent	487.0	89.0
Present	60.0	11.0
Endometrial grading		
A	96.0	18.3
B	408.0	77.9
C	20.0	3.8
Cause of infertility		
Both Male & Female	21.0	3.8
Female	308.0	56.3
Male	48.0	8.8
Unexplained	170.0	31.1
Level of physician		
Second-year fellow	63.0	11.5
Subspecialist	484.0	88.5
Semen analysis		
Abnormal	81.0	14.8
Normal	466.0	85.2
Protocol		
Antagonist	102.0	18.6
Long Agonist	156.0	28.5
Minimal stimulation	289.0	52.8
Uterine abnormality		
Absent	118.0	93.7
Present	8.0	6.3
Type of fertilization		
ICSI	292.0	53.4
IVF	255.0	46.6
Endometrial Morphology		
Non-trilaminar	5.0	0.9
Trilaminar	542.0	99.1
Previous pregnancy by the male		
None	176.0	84.2
One or more	33.0	15.8
Oocytes retrieved		
>5	406.0	76.9
<5	122.0	23.1
Pregnancy status		
Abortion	5	0.91
Biochemical Pregnancy	198	36.20
Clinical Pregnancy	21	3.84
Negative	323	59.05

Endometrial thickness measured on the day of hCG administration ranged from 5 to 14mm and pregnancy was achieved at each endometrial thickness value beyond 5mm(Table 2).

Table 2: Pregnancy rates at different endometrial thickness values

Endom Thickness	Pregnancy status		Pregnancy Outcome		
	Negative	Positive	BCP	CP	Ab
5	3	0	0	0	0
6	20	9	9	0	0
7	48	16	14	2	0
8	70	34	29	4	1
9	45	36	31	5	0
10	60	59	56	5	1
11	31	23	21	1	1
12	30	21	19	1	1
13	9	11	10	1	0
=>14	7	15	9	2	0
	323	224	198	21	5

BCP = biochemical pregnancy, CP= Clinical Pregnancy, Ab= Abortion

There was no statistical difference between those who could and couldn't achieve pregnancy in terms of the diagnosis and the duration of infertility, presence of uterine pathology, semen analysis abnormality, previous pregnancy by the male partner, endometrial morphology, type of fertilization, or level of physicians who performed the embryo transfer (Tables 3 and 4).

Compared to non-pregnant group according to bivariate analysis, the odd of pregnancy tends to be higher with age < 35y (84.4% vs 15.6%, p=0.04), AFC > 5 (p<0.001), a long agonist stimulation protocol (39.3% vs 21.1%, p<0.001), oocyte retrieval of >5, higher number of follicles on the day of hCG administration, day 3 and grade 1 embryos transfers (Tables 4 and 5). All except for the endometrial grading and day of embryo transfer have lost their significance when subjected to multivariate logistic regression analysis (Table 5).

Receiver operator curve (ROC) analysis

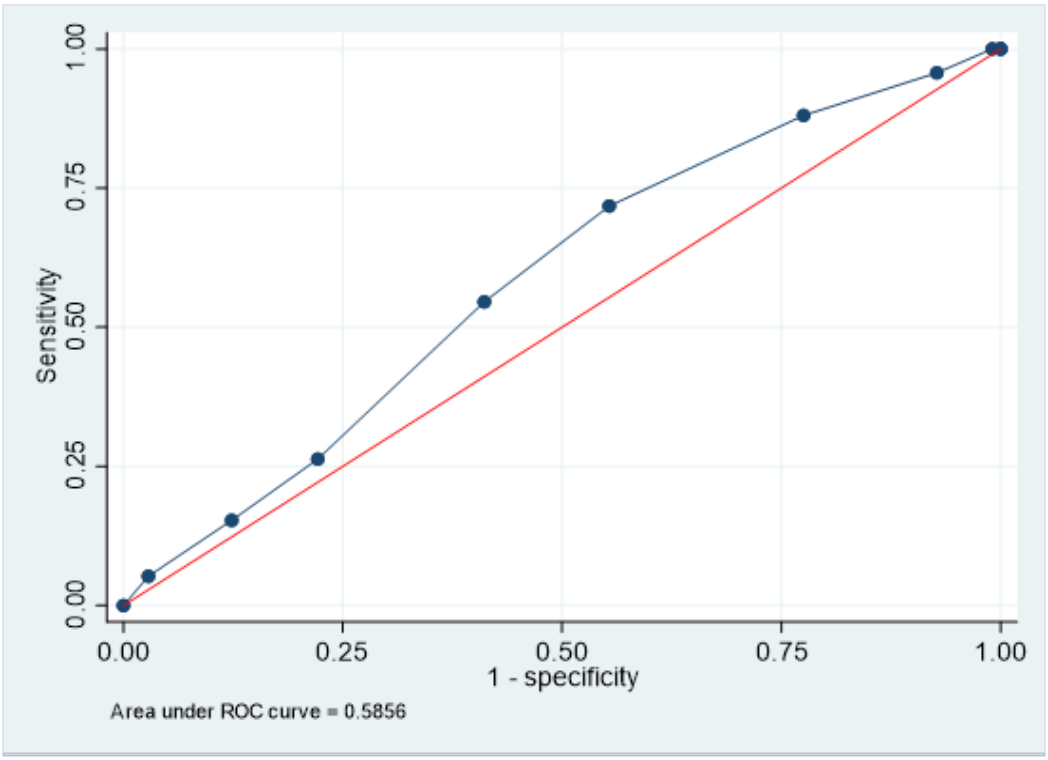


Table 3: Bivariate analysis of factors associated with pregnancy rate

Factor	Level	Negative (323)	Positive (224)	p-value
Age of the woman	<35y	286 (89.7%)	215 (96.0%)	0.007
	≥35y	33 (10.3%)	9 (4.0%)	
AFC	≥5	242 (75.9%)	193 (87.3%)	<0.001
	<5	77 (24.1%)	28 (12.7%)	
Duration of infertility(y)	<5	140 (45.0%)	116 (53.0%)	0.071
	≥5	171 (55.0%)	103 (47.0%)	
Adnexal pathology	Absent	287 (88.9%)	200 (89.3%)	0.87
	Present	36 (11.1%)	24 (10.7%)	
Endometrial grading	A	71 (22.5%)	25 (12.0%)	0.005
	B	235 (74.6%)	173 (82.8%)	
	C	9 (2.9%)	11 (5.3%)	
Cause of infertility	Both male & female	12 (3.7%)	9 (4.0%)	0.80
	Female	187 (57.9%)	121 (54.0%)	
	Male	26 (8.0%)	22 (9.8%)	
	Unexplained	98 (30.3%)	72 (32.1%)	
Level of physician	2nd year fellow	44 (13.6%)	19 (8.5%)	0.064
	Subspecialist	279 (86.4%)	205 (91.5%)	
Semen analysis	Abnormal	40 (12.4%)	41 (18.3%)	0.055
	Normal	283 (87.6%)	183 (81.7%)	
Type of protocol	Antagonist	66 (20.4%)	36 (16.1%)	<0.001
	Long Agonist	68 (21.1%)	88 (39.3%)	
	Minimal stimulation	189 (58.5%)	100 (44.6%)	
Uterine abnormality	Absent	70 (95%)	48 (92%)	0.60
	Present	4 (5%)	4 (8%)	
Type of fertilization	ICSI	182 (56.3%)	110 (49.1%)	0.095
	IVF	141 (43.7%)	114 (50.9%)	
Endometrial morphology	Non trilaminar	3 (0.9%)	2 (0.9%)	0.97
	Trilaminar	320 (99.1%)	222 (99.1%)	
Previous pregnancy by the male	None	105 (86.1%)	71 (81.6%)	0.38
	One or more	17 (13.9%)	16 (18.4%)	
Oocytes retrieved	>5	221 (70.4%)	185 (86.4%)	<0.001
	<5	93 (29.6%)	29 (13.6%)	
Day of ET	3	199 (79.9%)	117 (60.6%)	<0.001
	5	50 (20.1%)	76 (39.4%)	

Table 4. Bivariate analysis Comparisons of oocyte and embryo aspects between pregnant and nonpregnant women following a fresh embryo transfer (Bivariate analysis)

Factor	Negative	Positive	p-value
N	323	224	
Number of follicles on trigger, median (IQR)	6.0 (4.0, 10.0)	9.0 (5.0, 15.0)	<0.001
Eggs Retrieved, median (IQR)	5.0 (3.0, 11.0)	9.0 (5.0, 16.0)	<0.001
MII, median (IQR)	3.0 (2.0, 6.0)	6.0 (3.0, 12.0)	<0.001
Number of Embryo Transferred, median (IQR)	2.0 (2.0, 2.0)	2.0 (2.0, 2.0)	<0.001
EmbGr1, median (IQR)	1.0 (1.0, 2.0)	2.0 (1.0, 3.0)	<0.001
EmbGr2, median (IQR)	0.0 (0.0, 1.0)	1.0 (0.0, 2.0)	0.030
EmbGr3, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.23

Table 5: Multivariate logistic regression analysis of factors associated with a pregnancy rate

Factor	Level	Pregnancy test		AOR	p-value	95%	CI
		Negative (n=323)	Positive (n= 224)				
	<35y	286 (89.7%)	215 (96.0%)	1.00			
	≥35y	33 (10.3%)	9 (4.0%)	0.48	0.14	0.18	1.29
AFC	≥5	242 (75.9%)	193 (87.3%)	1.00			
	<5	77 (24.1%)	28 (12.7%)	0.77	0.38	0.43	1.38
Endometrial grading	A	71 (22.5%)	25 (12.0%)	1.00			
	B	235 (74.6%)	173 (82.8%)	1.91	0.03	1.07	3.43
	C	9 (2.9%)	11 (5.3%)	2.61	0.11	0.81	8.40
Level of physician	2nd yr. fellow	44 (13.6%)	19 (8.5%)	1.00			
	Subspecialist	279 (86.4%)	205 (91.5%)	1.53	0.21	0.79	2.95
Protocol	Antagonist	66 (20.4%)	36 (16.1%)	1.00			
	Long Agonist	68 (21.1%)	88 (39.3%)	1.63	0.14	0.85	3.13
	Minimal stimulation	189 (58.5%)	100 (44.6%)	1.40	0.27	0.77	2.56
Type of fertilization	ICSI	182 (56.3%)	110 (49.1%)	1.00			
	IVF	141 (43.7%)	114 (50.9%)	1.48	0.07	0.96	2.27
Endometrial morphology	Non trilaminar	3 (0.9%)	2 (0.9%)				
	Trilaminar	320 (99.1%)	222 (99.1%)	0.38	0.37	0.04	3.20
#of Embryo Transferred, (Median, IQR)		2.0 (2.0, 2.0)	2.0 (2.0, 2.0)	2.88	0.00	1.56	5.30
Day of embryo transfer	Day 3	199 (79.9%)	117 (60.6%)	1.00			
	Day 5	50 (20.1%)	76 (39.4%)	2.55	0.01	1.17	3.29

DISCUSSION

This study is the first of its kind in terms of addressing the issues of relation of endometrial thickness and pregnancy rate after fresh ET. The endometrial thickness at which most of the pregnancies in this study occurred falls in grade B group that ranged from 8 to 12 mm (82.8% vs 74.6%, p=0.05) and after controlling for the effects of multiple confounding factors using multivariate logistic regression analysis (p=0.02) it became evident that endometrial thickness has an independent relationship with pregnancy rate in this study.

Non-parametric Receiver-Operating Characteristic (ROC) analysis was carried out to identify the predictive ability of endometrial thickness on the pregnancy rate. Although the analysis indicated that endometrial thickness has a limited predictive ability of the pregnancy as evidenced by the areas under the curve (AUC) of 0.59 (95% CI= 0.53, 0.63) it was not possible to determine a cutoff of the endometrial thickness value with an acceptable trade-off between sensitivity and specificity.

Our findings were akin to the finding from other studies[6-10] including Richter et al, who indicated that EMT was greater in cycles resulting in pregnancy than in cycles not resulting in pregnancy and that clinical pregnancy and live-birth or ongoing pregnancy rates increase significantly with increasing endometrial thickness, independent of the effects of patient age and embryo quality.

Al-Ghamdi et al in their retrospective cohort study of 2464 cycles concluded that there is a positive linear relationship between the endometrial thickness measured on the day of hCG injection and PR and that endometrial thickness is independent of other variables[4].

Yuan indicated in a retrospective study, of 10,787 fresh IVF–ICSI treatment cycles that EMT is a significant and independent predictor of intrauterine pregnancy, ectopic pregnancy, spontaneous abortion and live birth after IVF–ICSI treatment[5].

Yang et al Combined analysis revealed those with endometrial thickness > 8mm and triple-line endometrial pattern had significant higher clinical pregnancy rates[6]. In a Canadian study of >22,000 fresh IVF-embryo transfer cycles, clinical pregnancy and livebirth rates were progressively lower with decreasing endometrial thickness. In fresh IVF-embryo transfer cycles, the livebirth rate decreased progressively per millimeter below 8mm[14].

On the other hand, studies have suggested that only the extremes of endometrial thickness values less than 8mm or greater than 14mm[15,16] negatively impact pregnancy rates. Many studies showed endometrial thickness of <6–7mm or >10–14 mm on hCG trigger day, has been reported to adversely affect implantation rate[11-13]. Our study has less to comment on the pregnancy outcome related with extremes of endometrial thickness values less than 8mm or greater than 14mm as their number is very small.

Regarding pregnancy outcomes when ET is above 14mm, results of studies are conflicting and more controversial. While some studies claim improved conception rate[9,14,15] others have reported a detrimental effect of a >14mm thick endometrium on conception rate[8]. Still other studies found no reduction in pregnancy rates with very thick linings[9]. A case report is widely cited describing a successful twin pregnancy in a woman with an endometrial stripe measuring 20mm[10].

According to some other studies if an endometrial thickness of at least 7mm cannot be attained, patients should be counselled for either continuing, or cancelling and subsequent frozen cycle while others recommend completion of all IVF cycles regardless of the thickness of the preovulatory endometrium. Accordingly a meta-analysis including 22 studies with a total of 10724 IVF–ICSI treatment cycles suggested that EMT cut-off of 7 mm has a limited capacity to identify pregnancy rates after IVF–ICSI and its use as a tool to decide on cycle cancellation, freezing of all embryos or refraining from further IVF treatment reported not to be justified[11].

On the other hand multiple studies have refuted the correlation between endometrial thickness and

pregnancy, and further went to suggest that neither individual nor combined analysis of EMT and pattern had predicting effects on live birth following IVF treatments, and embryo quality might be the one that really has effects[3].

Surprisingly, confounding effects of female age and number of oocytes retrieved according to regression were not associated with pregnancy prospects. This 'ecological fallacy' can be explained by the fact that our infertile women do not know their exact age and by inadequacy of our data.

DECLARATIONS

Limitations of the study

The study is retrospective, lacks adequate number of cases to comment on the pregnancy outcome of extremes of endometrial thickness values. Besides, as the data sources suffer from missing values our conclusions too were compromised.

Strength

This is the first attempt to review not only the relation of EMT in IVF in the country but also the role of possible confounders.

Conclusion and Recommendation

Current study indicates that EMT has a limited capacity to identify women who have a low chance to conceive after IVF. The frequently reported cut-off of 7mm is occurring infrequently. The use of EMT as a tool to decide on cycle cancellation, freezing of all embryos or refraining from further IVF treatment seems not to be justified based on EMT. Further research is needed to investigate the real independent significance of EMT in IVF in our setup.

Competing Interests

The author declares that he has no competing interests.

Funding

SPMMMC. The institution has no role in the design of the study, collection, analysis,
and interpretation of the data and in writing the manuscript.

Acknowledgement

My utmost gratitude goes to Dr Mekitie Wondafrash [(MD, PhD.) Research and Publication Adviser, St. Paul Institute for Reproductive Health and Rights] without whom the compiled data would have been mere numbers. I would like to thank, CFRM staffs for their continuous support during the survey. Above all I am indebted to my advisors and instructors and mentors Drs Mustafa, Thomas and Ayalew for their tireless constructive comments.

CORRESPONDING AUTHOR

Mutasim Abdullahi, MD, MPH
CFRM, SPHMMC, Addis Ababa Ethiopia
Email: mutasim347@gmail.com

REFERENCES

1. Liu KE, Hartman M, Hartman A. Management of thin endometrium in assisted reproduction: a clinical practice guideline from the Canadian Fertility and Andrology Society. Reprod Biomed Online [Internet]. 2019 Jul 1 [cited 2022 Feb 19];39(1):49–62. Available from: http://creativecommons.org/licenses/by-nc-nd/4.0/
2. Bu Z, Sun Y. The impact of endometrial thickness on the day of human chorionic gonadotrophin (hCG) administration on ongoing pregnancy rate in patients with different ovarian response. PLoS One. 2015 Dec 1;10(12).
3. Shakerian B, Turkgeldi E, Yildiz S, Keles I, Ata B. Endometrial thickness is not predictive for live birth after embryo transfer, even without a cutoff. Fertil Steril [Internet]. 2021;116(1):130–7. Available from: https://doi.org/10.1016/j.fertnstert.2021.02.041
4. Al-Ghamdi A, Coskun S, Al-Hassan S, Al-Rejjal R, Awartani K. The correlation between endometrial thickness and outcome of in vitro fertilization and embryo transfer (IVF-ET) outcome. Reprod Biol Endocrinol. 2008 Sep 2;6.
5. Yuan X, Saravelos SH, Wang Q, Xu Y, Li TC, Zhou C. Endometrial thickness as a predictor of pregnancy outcomes in 10787 fresh IVF–ICSI cycles. Reprod Biomed Online [Internet]. 2016;33(2):197–205. Available from: http://dx.doi.org/10.1016/j.rbmo.2016.05.002
6. Yang W, Zhang T, Li Z, Ren X, Huang B, Zhu G, et al. Combined analysis of endometrial thickness and pattern in predicting clinical outcomes of frozen embryo transfer cycles with morphological good-quality blastocyst: A retrospective cohort study. Medicine (Baltimore) [Internet]. 2018 Jan 1 [cited 2022 Mar 12];97(2). Available from: /pmc/articles/PMC5943888/
7. Richter KS, Bugge KR, Bromer JG, Levy MJ. Relationship between endometrial thickness and embryo implantation, based on 1,294 cycles of in vitro fertilization with transfer of two blastocyst-stage embryos. Fertil Steril. 2007 Jan;87(1):53–9.
8. Chan JM, Sukumar AI, Ramalingam M, Ranbir Singh SS, Abdullah MF. The impact of endometrial thickness (EMT) on the day of human chorionic gonadotropin (hCG) administration on pregnancy outcomes: a 5-year retrospective cohort analysis in Malaysia. Fertil Res Pr. 2018;4(1):1–9.
9. Dietterich C, Check JH, Choe JK, Nazari A, Lurie D. Increased endometrial thickness on the day of human chorionic gonadotropin injection does not adversely affect pregnancy or implantation rates following in vitro fertilization-embryo transfer.
10. Quintero RB, Sharara FI, Milki AA. Successful pregnancies in the setting of exaggerated endometrial thickness.
11. Wu Y, Gao X, Lu X, Xi J, Jiang S, Sun Y, et al. Endometrial thickness affects the outcome of in vitro fertilization and embryo transfer in normal responders after GnRH antagonist administration. Reprod Biol Endocrinol. 2014 Oct 9;12(1).

MAGNITUDE AND RISK FACTORS ASSOCIATED WITH ADOLESCENT PREGNANCY IN ETHIOPIA

Abebe Debu Liga[1], Adane Erango Boyamo[2], Yasin Negash Jabir[3]

ABSTRACT

Adolescent pregnancy occurs in girls aged between 13-19 years and is a major cause of newborn and maternal mortality in developing countries. This study examined the magnitude and risk factors associated with adolescent pregnancy in Ethiopia. The 2016 Ethiopian national representative survey was employed in the study. The sample of EDHS data was selected using a two-stage cluster sampling strategy. Descriptive statistics were developed using frequencies and percentages. The multilevel logistic regression approaches were then employed to determine the risk factors associated with adolescent pregnancy to factors that were shown to be significant at the 5% level in univariate analysis. The study found that the overall prevalence of adolescent pregnancy in Ethiopia was 10.26%. The finding also show that adolescent girls who were married at the age of less than 15 years (AOR: 3.14, 95% CI: 2.39, 4.14), between the ages of 15 and 17 years (AOR: 2.23, 95% CI: 1.59, 3.13), and who came from lower- or middle-class income households (AOR: 2.33, 95% CI: 1.55, 3.52), didn't use contraception (AOR: 18.46, 95% CI: 6.89, 49.49), and knew when their cycles were most fertile were more likely to become pregnant. In contrast, adolescent girls who achieved primary school and above, and exposed to media (AOR: 0.76, 95% CI: 0.56, 1.02) were associated to a lower risk of adolescent pregnancy. The finding indicated that adolescent pregnancy is a key public health concern in Ethiopia. Hence, the government should implement policies to limit the risks through formal education, and improve access to reproductive health education and contraception, especially among adolescent girls from the poorest households.

KEYWORDS: Adolescent pregnancy, Risk factors, Magnitude, Ethiopia

(The Ethiopian Journal of Reproductive Health; 2023; 15;25-35)

1 Department of Statistics, College of Natural and Computational Sciences, Wolkite University, Ethiopia
2 Department of Statistics, College of Natural and Computational Sciences, Wachamo University, Ethiopia
3 Department of Statistics, College of Natural Science, Jimma University, Ethiopia

INTRODUCTION

The World Health Organization (WHO) explained adolescence as the transition period between childhood and adulthood aged between 10-19 years[1]. According to the UNICEF, 2018 report, adolescent pregnancy occurs in girls between the ages of 13–19 years[2]. Nowadays, adolescent pregnancy remains a major public health concern worldwide and a leading cause of newborn and maternal mortality in developing countries[3]. In many cases, adolescents are not well informed about sexuality and reproductive health risks, making them vulnerable to early unwanted pregnancies, unsafe abortions, unplanned sexual practices, HIV infection, other sexually transmitted diseases (STIs), and, the physical and emotional challenges associated with adolescent pregnancy.

In Africa, the incidence of adolescent pregnancy is 18.8%, with approximately 19.3% in Sub-Saharan Africa[4] and more than 50% globally occurring in seven countries, including Ethiopia[5]. Annually, an estimated twenty one million and about 12 million girls, aged 15-19 years, become pregnant and give birth, respectively, in the least and middle-income countries[6]. Pregnancy-related difficulties and unsafe abortions also expose adolescent girls to a high risk of maternal mortality, morbidity, and neonatal complications[7-8] and also raise the risk of premature delivery, abnormal birth weight, late educational goals, and maternal depression[3].

Despite efforts aimed at reducing adolescent pregnancy and associated factors, it remains among the key sustainable development goals of the Ethiopian government. This goal is set to be achieved through the implementation of a law against early marriage, a national health strategy for adolescent and youth reproductive services; legalization of abortion; a policy on HIV/AIDS, and community mobilization against harmful traditional practices[9]. According to the EDHS-2016 report, the incidence of adolescent pregnancy was about 16% with a higher incidence rate occurring among rural residents[10]. Several studies identified factors associated with adolescent pregnancy such as early sexual intercourse[11,12], early marriage[13], place of residence[14,16], religion[14,15], age[15-18], employment[18,20], educational status[19,21-22], marital status[17-18], socioeconomic status[13-14,21-23], peer influence[21,22], use of contraceptives[11-12, 21], alcohol consumption[25], lack of comprehensive sexuality education[26], rape[27] and media exposure[23,24]. WHO, 2011 reported that adolescents less than 18 years of age have a 60% greater chance of losing their child in the initial years of life[28] and are highly probable to be exposed to marital violence[29]. Previous studies did not address regional and subject-specific variation in adolescent pregnancy between and within regions of Ethiopia using a nationally representative survey.

METHOD AND MATARIALS

Data Source, Study design, and Sampling

This study was performed use of the 2016 Ethiopian Demographic and Health Survey, a recent survey conducted in Ethiopia by the Central Statistical Agency between 1/18/2016 and 6/27/2016. The survey was done in all regions of Ethiopia using a community-based multistage stratified cluster sampling design with two phases covering 645 enumeration areas. Of the areas sampled for the study, 202 were from urban and 443 were from rural areas, considered the primary phase, and 28 households per cluster were made in the second phase. All men and women aged 15-59 were included in the interview. A total of 16,583 women were participated in the EDHS survey, of whom, 3,498 provided the data in this study[10].

Variables in the study

The outcome variable in this study was the status of adolescent pregnancy. It was coded as "1" when the adolescent become pregnant and "0" when they are not pregnant at the time of data collection. The independent variables considered for this study were age at first marriage, place of residence, marital status, early marriage, region, socio-economic status of parents, knowledge of the fertility window, exposure to mass media, employment, religion, use

of contraceptive method, and alcohol consumption.

Operational definitions

Socio-Economic Status (Wealth index): In numerous DHS and other country-level surveys, the wealth index has been used as a measure to highlight disparities in household characteristics, in the utilization of medical and other services, and in clinical outcomes. The resulting wealth index serves as a metric of wealth that is compatible with measures of income and spending. It divides the ranking into five equal portions, starting with quintile 1 (lowest) and ending with quintile 5 (richest or wealthiest). We divided the household wealth quintile into three categories for our study.

Inclusion and exclusion criteria

Adolescent girls aged between 10 to 19 years and who had full information's about pregnancy during the time of data collection were included, and adolescent's girls who lacks information's about pregnancy during the time of data collection were excluded from the investigation.

Methods of data analysis

Descriptive statistics like frequencies and percentages were used to explain the categories of predictors, and a Chi-square test of association was used to examine statistically significant predictors of adolescent pregnancy. Hosmer and Lemeshow's test of goodness of fit was used to measure the goodness of fit (The null hypothesis for the Hosmer and Lemeshow's test is the data fits the model well), while the Chi-square test for contingency was used to test whether there were systemic differences between the groups or regions[30]. Multilevel binary logistic regression models were employed to identify the effect and variations of pregnancy across the regional state of Ethiopia using the Stata statistical software: release 15 (College Station, TX: StataCorp LLC)[34]. In nested structure data like the Ethiopian demographic and health survey, the individual measurements have some degree of correlation within a cluster due to sharing common characteristics. Thus, when ignoring the correlation of the upper level and considering only the individual level characteristics leads to violating the assumption of independence between measurements. This result leads to an underestimation of standard errors, and biased parameter estimates, producing spurious significant results, and incorrect conclusions on effect sizes. In contrast, modeling individual-to-individual variation simultaneously with group-to-group variation analysis has numerous merits. It allows focusing on the importance of both communities' and individuals' effects on individuals' health outcomes[33]. Therefore, in this study, to get a fixed effect for both the individual and community-level factors and a random effect for the between cluster-variation, a two-level mixed-effect logistic regression analysis was used. In this study, a two-level logistic regression model was taken into account with the adolescent considered as level 1 and regions considered as level 2 to know the unexplained variation within groups and between groups. Three multilevel logistic regression models were examined hierarchically in this study, namely: a null model (model without predictors) or no explanatory variable that examined the total variance in the factors of pregnancy among regions; in model 2, only individual-level factors were included. Model 3 measured the combination of the effects of individual and regional-level factors.

The clustered nature of the data and the within and between community variations were taken into account by assuming each community had a different intercept and fixed coefficient. The amount of community variation was conveyed as intra-class correlation (ICC). The AIC, and BIC were used to choose a model that best explains the data, and the three fitted models with the lowest AIC and BIC value were taken.

RESULTS

Descriptive Statistics Results

In this study, 3498 adolescents from nine regional states falling within two administrative cities in Ethiopia were included. 10.26% of adolescents

had experienced pregnancy during the time of data collection. Of the pregnant adolescents, 8.27%, 20.68%, 7.04%, 13.73%, 15.36%, 10.55%, 6.91%, 15.57%, 14.21%, 1.85%, and 7.17% of them lived in Tigray, Afar, Amhara, Oromia, Somali, Benshangul, SNNPR, Gambella, Harari, Addis Ababa, and Dire-Dawa regions, respectively. 4.25% of urban adolescents and 13.59% of rural adolescents were pregnant during the time of data collection. Of the pregnant adolescents, 5.25% were Orthodox; 14.84% were Muslim, and 11.01% were of other religious faiths. 22.46% of pregnant adolescents had no formal education. 9.47% had primary education; 4.64% had secondary education, and 1.94% had higher education. Of pregnant adolescents, 14.13% were below 15 years of age at first marriage; 11.46% were aged 15-17, and 4.87% were aged 18 and above (table 1).

Table 1: Cross-tabulation between pregnancy status among adolescents and indicator variables

Variables	Categories	Not pregnant Count (%)	Pregnant Counts (%)	Chi-square Value	df	P-value
Region	Tigray	388 (91.73)	35 (8.27)			
	Afar	211 (79.2)	55 (20.68)			
	Amhara	330 (92.96)	25 (7.04%)			
	Oromia	358 (86.27)	57 (13.73)			
	Somali	270 (84.64)	49 (15.36)			
	Benishangul	212 (89.45)	25 (10.55)	101.88	10	0.000
	SNNPR	364 (93.09)	27 (6.91)			
	Gambela	179 (84.43)	33 (15.57)			
	Harari	157 (85.79)	26 (14.21)			
	Addis Adaba	424 (98.15)	8 (1.85)			
	Dire Dawa	246 (92.83)	19 (7.17)			
Residence	Urban	1193 (95.75)	53 (4.25)			
	Rural	1946 (86.41)	306 (13.59)	75.89	1	0.000
Age at first marriage	< 15 years	571 (85.87)	94 (14.13)	96.42	2	0.000
	15-17 years	1024 (88.54)	186 (11.46)			
	≥ 18 years	1544 (95.13)	79 (4.87)			
Religion	Orthodox	1335 (94.75)	74 (5.25)	71.499	2	0.000
	Muslim	1222 (95.16)	213 (14.84)			
	Others	582 (88.99)	72 (11.01)			
Educational status	No education	442 (77.54)	128 (22.46)	128.57	3	0.000
	Primary	1835 (90.53)	192 (9.47)			
	Secondary	761 (95.36)	37 (4.64)			
	Higher	101 (98.06)	2 (1.94)			
Socioeconomic status of family	Poor	992 (82.39)	212 (17.61)	128.54	2	0.000
	Middle	413 (87.87)	57 (12.13)			
	Rich	1734 (95.07)	90 (4.93)			
Knowledge of fertile window	During period	132 (89.8)	15 (10.20)	62.20	5	0.000
	After period	537 (81.86)	119 (18.14)			
	Middle time of period	592 (91.36)	56 (8.64)			
	Before period	237 (89.77)	27 (10.23)			
	Every time	707 (90.06)	78 (9.94)			
	Don't know	934 (93.59)	64 (6.41)			
Use of Contraceptives	No	3015 (91.72)	272 (8.28)	233.84	1	0.000
	Yes	124 (58.77)	87 (41.23)			
Employment Status	No	2342 (89.29)	281 (10.71)	2.30	1	0.129
	Yes	797 (91.09)	78 (8.91)			
	Female	1016 (90.31)	109 (9.69)			
Exposure to Mass Media	No	1321 (85.12)	231 (14.88)	64.684	1	0.008
	Yes	1818 (93.42)	128 (6.58)			
Early Marriage	No	2881 (95.9)	123 (4.1)	339.86	1	0.000
	Yes	358 (72.47)	136 (27.53)			
Alcohol consumption	No	3087 (90.32)	331 (9.68)	54.39	1	0.000
	Yes	52 (65)	28 (65)			

17.61% of pregnant adolescents were from poor family backgrounds; 12.13% were from middle socioeconomic and 4.93% were from wealthy family backgrounds. 10.20% perceived that they were fertile during the menstrual period, 18.14% at the end, 8.64% in the middle, 10.23% before, and 9.94% through the entire 30-day cycle, while 6.41% had no idea of when they were fertile. 41.23% of adolescents used contraceptives, while 8.28% did not use contraceptive methods. Moreover, 10.71% pregnant adolescent had non-employed while 8.91% had employed and 14.88% were non-exposed to mass media and 6.58% were exposed to mass media. Of the pregnant adolescent, 27.53% were married at early age while 4.1% were not married at early age; 35% of adolescent drank alcohol, while 9.68% did not drink alcohol.

Logistic Regression model Result

The Hosmer and Lemeshow test revealed that the p-value was greater than 0.05 and failed to reject the null hypothesis, and it indicated that the logistic model was suitable for the data (Table 2).

Table 2: Hosmer and Lemeshow Test

Hosmer and Lemeshow Test			
Step	Chi-square	Df	Sig.
1	7.825	8	0.451

Test of Heterogeneity

Using the Chi-square test ($p \leq 0.001$), we demonstrated significant heterogeneity between adolescent girls from different regional states of Ethiopia (Table 3).

Table 3: Tests of Heterogeneity

Chi-Square Tests			
Statistics	Value	Df	p-value
Pearson Chi-Square	101.880	10	0.000

Intra-correlation coefficients

The ICC in the null model was 0.1016, indicating that 10.16% of the total variation in the prevalence of adolescent pregnancy could be explained by the grouping structure in higher-level units or regions (Table 4).

Table 4: Summary results of model selection criteria and ICC

Class	Null model	Random intercept model	Random slope model
Deviance	72.02(p≤0.001)	409.7528(p≤0.001)	30.0107(p≤0.001)
AIC	2246.424	1864.671	1844.649
BIC	2258.744	1963.231	1974.008
ICC	0.1016461		

Results of Multilevel Binary Logistic Regression Model Associated with pregnancy status

Regional differences were more significantly associated with the level of education and use of contraceptives (Table 5).

Table 5: Confidence interval estimates of Random intercept and Random slope model

Random effects Parameters Region:Unstructured	Estimate	Std. Err.	[95% Conf. Interval]
Variance (Use of contraceptives)	2.046371	1.270492	[.6060591 6.909615]
Variance (Educational level)	0.194058	0.1339266	[.0501748 750546]
Variance (cons)	0.0214262	0.0375757	[.0006889 6663766]

The finding tells that age at first marriage, level of education, religion, socio-economic dynamics, use of contraceptives, knowledge of the fertility window, and media exposure were significantly associated with the risk factors associated with Adolescent pregnancy among adolescent girls in Ethiopia ($p<0.05$) (table 6).

Table 6: Multilevel Binary logistic regression results of predictors associated with Adolescent pregnancy

Variable	Category	Model 2 Odds Ratio (95% CI AOR)	Model 3 Odds Ratio (95% CI of AOR)	P-value
Age at first marriage	≥18 years	1	1	
	15-17 years	2.66(1.88, 3.77)	2.23(1.59, 3.13)	0.000
	< 15 years	3.53(2.62, 4.78)	3.14(2.39, 4.14)	0.000
Education	No education	1	1	
	Primary	0.49(0.36, 0.66)	0.43(0.28, 0.64)	0.000
	Secondary	0.36(0.22, 0.57)	0.26(0.12, 0.53)	0.000
	Higher	0.19(0.04, 0.82)	0.10(0.02, -0.59)	0.0260
Religion	Orthodox	1	1	
	Muslim	3.03(1.98, 4.62)	2.83(1.92, 4.17)	0.000
	Other	2.94(1.83, 4.73)	2.27(1.40, 3.69)	0.000
Socio-economic status of family	Rich	1	1	
	Middle	2.25(1.50, 3.36)	2.33(1.55, 3.52)	0.000
	Poor	2.81(1.99, 3.98)	2.88(2.03, 4.09)	0.000
Use of contraceptives	Yes	1	1	
	No	13.79(9.45,20.13)	18.46(6.89, 49.49)	0.000
Media Exposure	No	1	1	
	Yes	0.740(0.55, .99)	0.76(0.56, 1.02)	0.0490
Knowledge of fertile window	Do not know	1	1	
	During period	2.60(1.34, 5.05)	2.60(1.32, 5.15)	0.006
	After period	4.43(3.09, 6.34)	4.56(3.17, 6.56)	0.000
	Middle time of period	2.68(1.76, 4.08)	2.90(1.89, 4.46)	0.000
	Before period	3.02(1.76, 5.18)	2.98(1.71, 5.20)	0.000
	Every time	2.01(1.38, 2.92)	2.07(1.42, 3.02)	0.000
Constant		0.02(0.011, 0.035)	0.02(0.013, 0.040)	0.000

The finding revealed that adolescents first marriage aged 15-17 and first marriage < 15 were more likely to experience pregnant than those aged ≥18 (AOR: 2.23 (95% CI: 1.59, 3.13)), and (AOR: 3.14 (95% CI: 2.39, 4.14)) and that the odds of an adolescent who had primary, secondary, and higher education were less likely to experience childbirth than no formal education (AOR: 0.43 (95% CI: 0.28, 0.64), AOR: 0.26 (95% CI: 0.12, 0.53), and AOR: 0.10 (95% CI: 0.02, -0.59)) respectively.

The model showed that adolescents of Muslim and Other religions were more likely to experience pregnant than Orthodox followers (AOR: 2.83 (95% CI: 1.92, 4.17), and AOR: 2.27 (95% CI: 1.40, 3.69)) and that adolescent from poor and middle-income backgrounds was more likely to experience pregnancy than those from higher socioeconomic status (OR: 2.88 (95% CI: 2.03, 4.09) and AOR: 2.33 (95% CI: 1.55, 3.52)) respectively.

Similarly, adolescents who did not use contraceptive methods had higher odds of experiencing pregnancy than those from used contraceptives (AOR: 18.46 (95% CI: 6.89, 49.49)). The finding also showed that the log odds of an adolescent being exposed to mass media were less likely to practice pregnancy than those from non-exposed to media (AOR: 0.76 (95% CI: 0.56, 1.02)) holding the other factors constant in the model. The odds of adolescent

who had knowledge of the fertility window during their period, after their period, middle time of their period, before period, and every time were AOR: 2.60 (95% CI: 1.32, 5.15), AOR: 4.56 (95% CI: 3.17, 6.56), AOR: 2.90 (95% CI: (1.89, 4.46), AOR: 2.98 (95% CI: 1.71, 5.20), AOR: 2.07 (95% CI: 1.42, 3.02) times more likely to experience pregnancy than adolescent with no knowledge about fertile time.

DISCUSSION

This study assessed the magnitude and risk factors associated with pregnancy among adolescent girls in Ethiopia. The results were consistent with previous reports from related studies. Adolescent girls who lived in Afar, Gambella, Somali, Harari, and Oromia regions had higher pregnancy rates than those in Benishangul-Gumuz, Tigray, Dire Dawa, Amhara, SNNPR, and Addis Ababa. This is likely a result of regional differences in cultural and religious variations in values towards reproduction, sexuality and marriage.

Using a multilevel binary logistic model, we demonstrated that age at first marriage, education, religion, socio-economic status, the use of contraceptives, knowledge of the fertile window during the menstrual cycle, and media exposure were significantly associated with adolescent pregnancy in Ethiopia. There were no studies at the national level that did address regional and subject-specific variation in adolescent pregnancy. Therefore, this study examines the heterogeneity between pregnancies among adolescent girls from different regional states of Ethiopia and also explored about the magnitude and the risk factors associated with pregnancy. The finding showed that the risk of adolescent pregnancy was higher among early married adolescent, is consistent with reports by Presler-Marshall and Jones (2012) that revealed early marriage increased the likelihood of adolescent pregnancy[13] and also supports with previous reports that revealed early sexual intercourse was a predictor of increasing adolescent pregnancy[11-12]. The possible reason for this might be that early marriage results in repeated births in less than 24 months, multiple unwanted pregnancies, termination of pregnancy, and early sterilization due to absence of access to contraceptives.

The findings of this study also revealed that education had a significant effect on the risk of adolescent pregnancy. This observation is also consistent with reports by Habito et al (2019) and Eyasu (2016) that uneducated adolescent had an increased incidence of adolescent pregnancy[21,31] and with the CSA, 2016 report that increased the level of education was associated with lower chance of exposure to adolescent pregnancy[10]. Reports by Worku et al (2021) showed that the chance of pregnancy was lower among girls who achieved secondary and higher education[22].

The observation that adolescents from poor and middle-income families were more likely to be exposed to adolescent pregnancy is consistent with reports by Mathewos, and Mekuria (2018) that adolescents who lived with poor parents were more likely to experience adolescent pregnancy[15]. Similar observations have been reported elsewhere[11-12] and could be explained to a certain extent due to the fact that adolescents from wealthy families are more likely to get formal education and access to convectional contraceptives where applicable. Like in this study, exposure to media had previously been reported to have an impact on the risk of adolescent pregnancy[23,24].

The odds of adolescents that do not use contraceptive methods have higher odds of experiencing adolescent pregnancy than those using contraceptive methods is in line with the report of Mathewos, and Mekuria (2018) that the non-use of contraceptives increased the likelihood of adolescent pregnancy[15] and is also consistent with a previous report by Morón-Duarte et al (2018) that a low level of contraceptive utilization increased adolescent pregnancy[11].

Surprisingly, the odds of experiencing pregnancy among adolescents who had an idea of when they had been fertile were higher than those with no idea of fertile time. This finding contradicts a previous

report conducted by Mezmur et al (2021) that the risk of adolescent pregnancy was higher among adolescents with no idea of fertile time[32] and the possible reason might be due to they have less desire to use contraceptives and have the desire to have a child on time.

The findings may therefore contribute to preventative programs and strategies by offering current information for program implementation and decision-making at both the individual and community levels to reduce the risk of adolescent pregnancy..

CONCLUSION

This study demonstrated 10.26% prevalence of adolescent pregnancy in Ethiopia and association with cultural practices as well as socioeconomic status of parents. The study also show that adolescent girls who were married at the age of less than 15 years, between the ages of 15 and 17 years, and who came from lower- or middle-class income households, didn't use contraception, and knew when their cycles were most fertile were more likely to become pregnant. Contrary, adolescent girls who achieved primary school and above, and exposed to media was associated to a lower risk of adolescent pregnancy. This study reveals that adolescent pregnancy is one of public health concern in Ethiopia. Hence, the government should implement policies to limit the risk through formal education, improved access to reproductive health education and contraception, especially among adolescent girls from the poorest households.

DECLARATIONS

Abbreviations

UNICEF: United Nations Children Fund; WHO: World Health Organization; OR: Odds Ratio, CSA: Central Statistical Agency; EAs: Enumeration Area; EDHS: Ethiopian Demographic and Health Survey; SSAR: Sub-Saharan African regions; HIV: Human Immune Virus and STI: Sexually Transmitted Diseases.

Acknowledgments

The authors would like to thank Ethiopian Central Statistical Agency (CSA) for providing the EDHS 2016 dataset. The authors have also appreciated all experts and research assistants who retained the study.

Declaration of interests

All authors declare no conflict of interest related to the material presented in this study.

Funding statement

No funding was provided for this study.

Authors' contributions

All authors played a significant role in designing the study, data analysis, interpretation, drafting, revising the article, and accepting all aspects of the work.

Availability of data and materials

The dataset is available through the CSA website: http://www.statsethiopia.gov.et.

CORRESPONDING AUTHOR

Abebe Debu Liga
Department of Statistics, College of Natural and Computational Sciences, Wolkite University, Ethiopia
Email address: abe.debu@yahoo.com

REFERENCES

1. Gollogly L. World health statistics 2009. World Health Organization; 2009.
2. United Nations Children's Fund, UNICEF. Report on the regional forum on adolescent pregnancy, child marriage and early union in south-east Asia and Mongolia; 2018.
3. World Health Organization. Global health estimates 2016: deaths by cause, age, sex, by country and by region, 2000–2016. Geneva: World Health Organization. 2018 Nov.
4. Kassa GM, Arowojolu AO, Odukogbe AA, Yalew AW. Prevalence and determinants of adolescent pregnancy in Africa: a systematic review and meta-analysis. Reproductive health. 2018 Dec; 15(1):1-7.
5. United Nations Economic Commission for Africa (UNECA), African Union, African Development Bank Group U. Assessing Progress in Africa toward Development Goals the Millennium: Food security in Africa: Issues, challenges and lessons. Addis Ababa: UNECA; 2013.
6. Darroch J, Woog V, Bankola A, Ashford L. Adding It Up: Costs and Benefits of Meeting the Contraceptive Needs of Adolescents. New York: Guttmacher Institute; 2016.
7. Loaiza E, Liang M. Adolescent pregnancy: a review of the evidence. Unfpa; 2013.
8. Abbas AM, Ali SS, Ali MK, Fouly H, Altraigey A. The maternal and neonatal outcomes of teenage pregnancy in a tertiary university hospital in Egypt. Proceedings in Obstetrics and Gynecology. 2017 Oct 1;7(3).
9. Ayele BG, Gebregzabher TG, Hailu TT, Assefa BA. Determinants of teenage pregnancy in Degua Tembien District, Tigray, Northern Ethiopia: A community-based case-control study. PloS one. 2018 Jul 25; 13(7):e0200898.
10. Csa I. Central statistical agency (CSA)[Ethiopia] and ICF. Ethiopia demographic and health survey, Addis Ababa, Ethiopia and Calverton, Maryland, USA. 2016; 1.
11. Morón-Duarte LS, Latorre C, Tovar JR. Risk factors for adolescent pregnancy in Bogotá, Colombia, 2010: a case-control study. Revista Panamericana de Salud Pública. 2014 Sep; 36(3):179-84.
12. Santos MI, Rosario F. A score for assessing the risk of first-time adolescent pregnancy. Family practice. 2011 Oct 1; 28(5):482-8.
13. Presler-Marshall E, Jones N. Empowering girls to prevent early pregnancy. Oversees Development Institute. 2012 Jul.
14. Nalenga GZ. Causes of unintended pregnancy among adolescents in Addis Abeba. Ethiopia: Norwegian University of Life Sciences. 2012 May.
15. Mathewos S, Mekuria A. Teenage pregnancy and its associated factors among school adolescents of Arba Minch town, southern Ethiopia. Ethiopian journal of health sciences. 2018; 28(3):287-98.
16. Ayanaw Habitu Y, Yalew A, Azale Bisetegn T. Prevalence and factors associated with teenage pregnancy, Northeast Ethiopia, 2017: a cross-sectional study. Journal of pregnancy. 2018 Nov 1; 2018.
17. Ayele BG, Gebregzabher TG, Hailu TT, Assefa BA. Determinants of teenage pregnancy in Degua Tembien District, Tigray, Northern Ethiopia: A community-based case-control study. PloS one. 2018 Jul 25; 13(7):e0200898.
18. Nwosu UM. Contemporary factors of teenage pregnancy in rural communities of Abia state, Nigeria. International Journal of Community Medicine and Public Health. 2017 Feb; 4(2):588-92.
19. Alemayehu T, Haidar J, Habte D. Utilization of antenatal care services among teenagers in Ethiopia: a cross sectional study. Ethiopian Journal of Health Development. 2010; 24(3).
20. Ezegwui HU, Ikeako LC, Ogbuefi F. Obstetric outcome of teenage pregnancies at a tertiary hospital in Enugu, Nigeria. Nigerian journal of clinical practice. 2012; 15(2):147-50.
21. Eyasu AM. Determinants of adolescent fertility among Rural Women of Ethiopia. Open Access Library Journal. 2016 Mar 31; 3(3):1-9.
22. Worku MG, Tessema ZT, Teshale AB, Tesema GA, Yeshaw Y. Prevalence and associated factors of adolescent pregnancy (15–19 years) in East Africa: a multilevel analysis. BMC Pregnancy and Childbirth. 2021 Dec; 21(1):1-8.
23. Fatema K, Lariscy JT. Mass media exposure and maternal healthcare utilization in South Asia. SSM-Population Health. 2020 Aug 1; 11:100614.
24. Bain LE, Muftugil-Yalcin S, Amoakoh-Coleman M, Zweekhorst M, Becquet R, de Cock Buning T. Decision-making preferences and risk factors regarding early adolescent pregnancy in Ghana: stakeholders' and adolescents' perspectives from a vignette-based qualitative study. Reproductive Health. 2020 Dec; 17(1):1-2.
25. Panova OV, Kulikov AM, Berchtold A, Suris JC. Factors associated with unwanted pregnancy among adolescents in Russia. Journal of pediatric and adolescent gynecology. 2016 Oct 1; 29(5):501-5.

26. Atuyambe LM, Kibira SP, Bukenya J, Muhumuza C, Apolot RR, Mulogo E. Understanding sexual and reproductive health needs of adolescents: evidence from a formative evaluation in Wakiso district, Uganda. Reproductive health. 2015 Dec; 12(1):1-0..
27. Yakubu I, Salisu WJ. Determinants of adolescent pregnancy in sub-Saharan Africa: a systematic review. Reproductive health. 2018 Dec; 15(1):1-1.
28. World Health Organization. Department of maternal, newborn, child and adolescent health (MCA): progress report 2014–15.
29. Loaiza E, Liang M. Adolescent pregnancy: a review of the evidence. Unfpa; 2013.
30. Hosmer Jr DW, Lemeshow S, Sturdivant RX. Applied logistic regression. John Wiley & Sons; 2013 Apr 1.
31. Habito CM, Vaughan C, Morgan A. Adolescent sexual initiation and pregnancy: what more can be learned through further analysis of the demographic and health surveys in the Philippines?. BMC public health. 2019 Dec; 19(1):1-3.
32. Mezmur H, Assefa N, Alemayehu T. Teenage pregnancy and its associated factors in eastern Ethiopia: a community-based study. International Journal of Women's Health. 2021; 13:267.
33. Goldstein H. Multilevel statistical models. John Wiley & Sons; 2011 Jul 8.
34. StataCorp L. Stata statistical software: Release 15 (2017). College Station, TX: StataCorp LP. 2017.

RATE OF CESAREAN DELIVERY AMONG PHYSICIANS PRACTICING IN A TEACHING HOSPITAL IN TIGRAY REGION, NORTHERN ETHIOPIA

Hale Teka[1], Awol Yemane[1], Sumeya Ahmed[1], Ephrem Berhe[1], Mebrihit Gebremeskel[1]
Hiluf Ebuy Abraha[1], Abida Hasan[2], Ermias Abate[1]

ABSTRACT

INTRODUCTION: The Ethiopian national cesarean section rate is about 5%. Rates of cesarean delivery (CD) vary widely among population segments in Ethiopia suggesting unequal access. Within this context, this study aimed to assess the rate of CD among physicians practicing at Ayder Comprehensive Specialized Hospital (ACSH).

METHODS: This was cross-sectional study. All female physicians who are parous (n = 15) and all male physicians whose spouses are parous (n = 86) were interviewed to evaluate the mode of delivery among them. Indications for CD were also assessed.

RESULTS: The overall CD rate among participants was 81 (44.3%). Thirteen out of 18 (87%) female obstetrician/gynecologists and male obstetrician/gynecologists' spouses delivered via CD. Cesarean delivery for maternal request (CDMR) accounted for 22.6% of primary CDs. Nearly all (95%) potential candidates for Trial of Labor after Cesarean delivery (TOLAC) opted for repeat elective CD. The driving factors for CD were: lack of confidence in the process of intrapartum fetal monitoring, "uncertainty" of outcome of vaginal delivery, fear of labor pain (due to absence of labor analgesia), and managing obstetricians' fear of blame for poor outcome by their colleagues.

CONCLUSION: This study revealed a disparity in CD rates in physician community vs the general Ethiopian population. More revealing are the reasons why they underwent CD. Rate of CD may be decreased by winning the confidence of the parturient mothers through instituting international-standard intrapartum fetal monitoring and labor analgesia protocols.

KEY WORDS: Rate of Cesarean Delivery, Mode of delivery, Indication, Cesarean Delivery for Maternal Request, Physicians

(The Ethiopian Journal of Reproductive Health; 2023; 15;36-46)

1 Mekelle University, College of Health Sciences, Ayder Comprehensive Specialized Hospital, Tigray, Ethiopia
2 Baylor College of Medicine, Baylor, Houston, Texas, USA

INTRODUCTION

Cesarean delivery (CD) is the most common lifesaving major surgery performed worldwide[1]. Rates continue to rise globally, and CD now accounts for more than 1 in 5 (21%) of all childbirths[2]. Rates range from 9.2% in Africa to 39.3% in the Americas[2]. The World Health Organization (WHO) predicts that a third of all deliveries (29%) will occur via CD in 2030[3]. On average, rates of sub-Saharan Africa are about 5%, indicating underuse, while the average rate of 42.8% in Latin America and the Caribbean suggests overuse[2]. These rates also reveal existing disparities in access to this lifesaving procedure.

In Ethiopia, rates of CD in urban and rural settings are 24% and 1% respectively[4]. The rates in hospitals in major cities and private for-profit organizations mirror the rates in developed countries. The stark variation in CD rates in low-middle income countries (LMIC) is multifactorial. The poorest subpopulations in Ethiopia may not have access to safe CD due to proximity/distance from hospitals, poverty contributing to challenges with obtaining prenatal care, and poor health literacy contributing to a lack of awareness of the need for medical attention. By contrast, high rates of CD in urban areas denote a degree of relative privilege that includes access to CD, prenatal care, and improved health literacy in the context of healthcare in Ethiopia[5].

Reasons cited for the global increasing trend in CD rates include higher financial incentives for physicians performing CD, maternal request, and lack of regulations on indications for the procedure [6]. When performed for medically justifiable indications, CD can improve maternal and neonatal outcomes. However, there is no maternal or neonatal benefit when performed without maternal or fetal indication[7]. Moreover, when performed for medically unindicated reasons, the risks may outweigh the benefits. In the absence of maternal or fetal indications, CD can be harmful to both the mother and the baby[8].

The safety of CD has improved dramatically over time. However, as in any major surgery, it still possesses short- and long-term complications[9]. Short-term complications include re-laparotomy, anesthesia-related morbidities, adjacent organ injuries (bladder, bowel, and vascular), increased risks of thromboembolic complications, an increased hospital stay, and surgical site infections[7,10]. Long-term maternal complications include a high rate of repeat CDs, adhesion, scar dehiscence, uterine rupture, adherent placentation, and risks of peripartum hysterectomy in subsequent deliveries[7,11,12].

One population that arguably has the readiest access to obstetric care and CD and the highest degree of health literacy is physicians. An interesting query that underlies the ethics and equity of obstetric delivery of care might be, "how do physicians give birth?" With knowledge about complications inherent in major surgeries, it may be assumed that physicians would avoid medically unindicated CD. Congruent with this assumption, a study by Johnson et al. revealed that physicians, as compared to their nonphysician counterparts, are more likely to deliver vaginally[13]. So far, some studies have assessed the preferred mode of delivery among medical professionals[14]. However, to our knowledge, there is no accessible data that shows the actual mode of delivery among physicians in the sub-Saharan context. This cross-sectional study aims to assess the actual mode of delivery of physicians practicing in a teaching hospital in the Tigray region of Ethiopia.

OBJECTIVE

The objective of this study is to determine the rate of Cesarean delivery (CD) among parous physicians and their partners at Ayder Comprehensive Specialized Hospital (ACSH) in 2018.

METHOD AND MATERIALS

Research Design

A cross-sectional survey was conducted in 2018, wherein 101 eligible participants were recruited and

surveyed. A medium effect size of 0.3 was used to compute statistical power to ensure adequate sample size. Therefore, this sample size yields a power of 85.5%, which is greater than the conventional 80% statistical power for a 95% CI.

Setting

The study was carried out at ACSH in 2018, which is a teaching hospital serving as a referral catchment area for over 8 million people. Fetal monitoring in ACSH features both Pinard Stethoscope intermittent use of electronic fetal monitoring machines to assess fetal heart rate but without the ability to assess fetal heart rate pattern or tracing. Pain management during labor is not provided.

Participants

The participants for this study were parous resident/ senior physicians practicing at ACSH.

Ethical Approval and Consent to Participate

Ethical approval was obtained from the Health Research Review Committee of Mekelle University, College of Health Sciences. Informed consent was obtained from the participants for data collection interviews.

Data Collection

A questionnaire was developed from a literature review. It contains variables such as socio-demographic variables, indications for CD, reasons for choosing CD, and the future plan for Trial of Labor after Cesarean (TOLAC) in those who are candidates. It was pretested on senior physicians at Adigrat General Hospital in 2018. Two obstetrics and gynecology residents were trained as data collectors, and data was collected through a structured and previously established questionnaire.

Data Analysis

The data was entered into IBM SPSS statistics data editor version 20. Descriptive statistics such as mean with standard deviation for continuous variables and proportions for categorical variables were used. Frequency tables were produced and analyzed for demographic and clinical variables.

RESULTS

In the present study, 101 physicians practicing at ACSH participated. Majority (n =70, 69.3%) were senior physicians, and the remaining (n=31, 30.7%) were resident physicians (Table 1). The age of the study participants ranged from 26 – 55 years with a mean age of 35±6.3 years. A total of 183 deliveries were registered. Among these, 181 were singleton, and two were twin deliveries. Parity of the study participants ranged from 1 to 5 with mean parity of 1.81±0.9.

Table 1: - Sociodemographic characteristics of physicians practicing at ACSH, 2018

Variables	Categories	Frequency	Percent
Sex	Males	86	85.1%
	Females	**15**	**14.9%**
Marital status	Married	98	97%
	Others	3	3%
Department	Surgery	31	30.7%
	Internal Medicine	27	26.7%
	Obstetrics and Gynecology	18	17.8%
	Pediatrics	14	13.9%
	Radiology	6	5.9%
	Dermatology	4	4.0%
	ENT	1	1.0%
Academic Rank	Resident	31	30.7%
	Senior	70	69.3%
Occupation of Partner	Health professional	70	69.3%
	Not health professional	31	30.7%
Place of Delivery	Governmental institution	179	95.2%
	Private institution	9	4.8%
Parity	1	43	42.6%
	2	39	38.6%
	3	15	14.9%
	4	3	3.0%
	5	1	1.0%

In this study, CD accounted for 44.3% (n=81) of the overall 183 deliveries. Rate of CD during the birth of the first child was 45.5% (n = 46 CD) (Table 2).

Table 2: - Mode of delivery among physicians and/or partner of physicians practicing at ACSH, 2018.

Mode of Delivery[1]		1st Child	2nd Child	3rd Child	4th Child	5th Child
Vaginal Delivery	Number	55	30	14	3	0
	Frequency	54.5%	51.7%	73.7%	75%	0
Cesarean Delivery	Number	46	28	5	1	1
	Frequency	45.5%	48.3%	26.3%	25%	100%

1 Total CD deliveries (n=81), primary CD (n=53) on which (n=28) repeat CDs were done)

The most common indications for primary CD were maternal request 12 (22.6%) , poor progress of labor 11 (20.6%), and oligohydramnios 10 (19.9%). The most common indications for repeat CD were maternal desire for repeat CD 19 (67.8%), history of 2 prior CDs 5 (17.9%), and previous myomectomy scar with 1 previous CD scar 2(7.1%) (Table 3).

Table 3: Type and indications for CD among physicians and/or partners of physicians practicing at ACSH, 2018 (n=81)

Type	Frequency	%
Primary Cesarean Delivery		
1. Maternal request for CD	12	22.6%
2. Poor progress of labor	11	20.6%
3. Oligohydramnios	10	19.0%
4. Fetal macrosomia	7	13.2%
5. Nonreassuring fetal heart rate status	6	11.3%
6. Malpresentation	3	5.7%
7. Previous myomectomy scar	2	3.8%
8. Antepartum hemorrhage	1	1.9%
9. Preeclampsia with unfavorable Bishop score	1	1.9%
Total	53	100%
Second Cesarean Delivery		
1.Opted for repeat CD Scar	19	82.6%
2.Failed TOLAC	1	4.4%
3.APH with Previous CD Scar	1	4.4%
4.Previous myomectomy scar + 1 Previous CD Scar	2	8.6%
Total	23	100%
Third Cesarean Delivery	**5**	**100%**

Nearly all (95%) candidate for TOLAC opted for repeat elective CD. There were 30 physicians with only 1 previous CD scar at the time of the interview. Among these, 21 (70%) had the intention to try labor on subsequent deliveries 1 parturient was uncertain for the preferred mode of delivery in the subsequent pregnancy.

Among 12 mothers who underwent CD for maternal request 41.7% opted for CD because they do not trust the process of intrapartum fetal monitoring in the absence of continuous electronic fetal monitoring. A similar number of women opted CD for fear of labor pain. Half (50%) of study participants with oligohydramnios thought vaginal delivery would confer greater peripartum risk than CD in the set up where this study was conducted. Nearly 30% of participants who underwent CD thought their physician was influenced to perform CD because the parturient was a physician (Table 4).

Table 4: Circumstances during primary CD among physicians and/or partners of physicians practicing at ACSH, 2018

Variable	Response	Frequency	%
1. Alternative mode of delivery provided	Yes	36	67.9%
	No	17	32.1%
2.Treating physician influenced into CD	Yes	16	30.2%
	No	30	56.6%
	Uncertain	7	13.2%
3.Relationship with the surgeon	Close friend	16	30.2%
	Colleague	26	49.1%
	No relationship	11	20.8%
4.Mother or partner Requested for CD	Yes	20	37.7%
	No	33	62.3%
5.Reasons for choosing CD (for those who underwent CD for maternal request)	Lack of confidence in vaginal delivery due to lack of electronic intrapartum fetal monitoring	05	41.7%
	Fear of labor pain	05	41.7%
	Vaginal delivery brings more harm to the baby than CD	01	8.3%
	For timed delivery	01	8.3%
6. Reasons for choosing CD (for those who had CD done for oligohydramnios)	Lack of trust in the vaginal delivery owing to lack of electronic intrapartum fetal monitoring	3	30%
	Fear of labor pain	1	10%
	Vaginal delivery brings more harm to the baby than CD	5	50%
	Indicated	1	1%
Complications related to CD	Yes[2]	8	15.1%
	No	45	84.9%

2 Spinal headache = 3, surgical site pain = 2, high spinal = 1, PPH = 1, and Paralytic ileus = 1

Nearly three- fourths of the study participants believed that the rate of CD among physicians is higher than the general population. Approximately two- third of them thought CD in this group are performed for maternal request. Nearly 85% of study participants agree that the parturient is biased toward CD because of one or combinations of factors specific to ACSH (Table 5).

Table 5: Attitude of physicians practicing at ACSH towards CD

Variable	Response	Frequency	%
1. CD done on physician parturient	They are mostly done for rational indications	24	23.8
	They are mostly done not for justifiable medical indications	64	63.4
	Uncertain	13	12.9
2.Rate of CD in physicians as compared to the general population	**High**	**73**	**72.3%**
	Same	9	8.9%
	Low	9	8.9%
	Uncertain	10	9.9%
3.Complications of CD as compared to vaginal delivery	Better	21	20.8%
	Neutral	47	46.5%
	Worse	33	32.7%
4. CD for maternal request	Strongly support	13	12.9%
	Support	17	16.8%
	Undecided	6	5.9%
	Do not support	43	42.6%
	Strongly do not support	22	21.8%
5.Reasons for choosing CD over vaginal delivery	Lack of trust in the vaginal delivery owing to lack of electronic intrapartum fetal monitoring	07	6.9%
	Fear of labor pain	07	6.9
	Vaginal delivery brings more harm to the baby than cesarean delivery	10	9.9%
	For timed delivery	02	2.0%
	Combinations of the above factors	59	58.4%
	They are done for indications	16	15.8%

DISCUSSION

In the present study, 45.5% of physicians gave birth to their first child via CD. Similarly, the overall CD rate was 44.3%. This is in stark contrast to the 5.4% national average of the CD rate in Ethiopia[15]. The rate is still higher than the overall national institutional CD rate, which is 18%[16]. In 2016, the CD rate in ACSH was 33.5% with an average annual increment of 1.7%[17]. Rates of CD in urban and rural settings in Ethiopia are 24% and 1%, respectively[4]. Higher CD rates in physicians than the general population contradicts the findings of a study conducted in the US which revealed physicians get fewer cesarean deliveries than non-physician counterparts[13]. The rate in this study was also higher than the findings of a study in Finland which showed a 15.9% overall CD rate among physicians[18]. The discrepancy may be explained by the differences with CD costs in different settings. All maternity services, including CD, are provided for free in Ethiopia. In contrast, mothers pay for CD in both the US and the Finland studies leading parturient physicians to tilt towards vaginal delivery to avoid the high cost incurred as a result of having a CD.

CDMR was the commonest (26.6%) indication for primary CD. Ironically, two-thirds of the study participants in this study do not support Cesarean section to be done for maternal request. Poor progress of labor and oligohydramnios accounted for 20.6% and 19.9% of primary cesarean deliveries. This contradicts a study conducted by Gedefaw et al., which showed cephalopelvic disproportion, non-reassuring fetal heart rate pattern, and obstructed labor to be the commonest indications in Ethiopia[19]. This result also contrasts with the commonest indications in another study conducted in ACSH, which depicted non-reassuring fetal heart rate pattern, cephalopelvic disproportion, and repeat cesarean deliveries to be the commonest indications[17]. In our study, the CD was not done for classic indications, as maternal request prevails as an indication. This may explain the divergences from the commonest indications as compared to previous reports.

Of all CDs in the present study, CDMR accounted for 14.3%. This rate is lower than the rate of CDMR in China (22.3%)[20]. However, the rate of CDMR in the current study was significantly higher than other high-income and LMIC studies. Studies in USA and Canada revealed CDMR rates of 3.9% and 2.5%, respectively[21, 22]. One systematic review of LMIC countries showed a CMDR rate of 2% [23]. The difference might be related to the fact that as participants in this study are physicians and as a result have easy access to CD services compared to the general population in other studies.

The reasons for choosing CD in those who underwent CDMR were the absence of electronic fetal monitoring and fear of labor pain. A study in India similarly points out that patients underwent CDMR for reasons of painless labor[24]. A study by Zhao et al. revealed that lack of confidence in vaginal birth is the single most important factor influencing women for CDMR[25].

The practice of offering CDMR is discouraged by several authorities[26]. CD is a major surgery with multiple complications. There is a lack of evidence that CD brings benefit for low-risk pregnancies. CD is associated with increased hospital stay and healthcare cost, and complications in subsequent pregnancies such as morbidly adherent placentation, uterine rupture, and hysterectomy[27, 28]. There is emerging evidence that babies born by CD have different hormonal, physical, bacterial, and medical exposures, and that these exposures can subtly alter neonatal physiology[27,28]. Thus, it should be reserved only when there is a perceived risk that impedes the life of the mother and/or the baby which can be offset with the application of CD[29,30].

Half of the study participants with oligohydramnios thought vaginal delivery brings more harm than CD in the setting where this study was conducted. However, several pieces of evidence show that isolated oligohydramnios is not typically a direct indication for CD[31,32]. It is noteworthy that adequate intrapartum fetal monitoring may be a contingency upon which the risk of harm from vaginal delivery may arise.

Strengths and Limitations of the Study

This study assessed a rarely addressed research question and can be used as a baseline on which future studies can base to examine reasons for the high prevalence of Cesarean Delivery among physicians. However, it has several limitations. First, it did not have comparative group. Rate of Cesarean delivery among physicians was compared against rates of previous studies in different settings and contexts. Second, the cross-sectional design of the study does not allow for causal inference or the examination of changes over time. Third, the findings may not be generalizable to other settings with different fetal monitoring and pain management practices during labor. Fourth, the data collected were self-reported, which may be subject to recall bias and may not accurately represent the actual practices or behaviors of the participants.

CONCLUSION

This study revealed a disparity in CD rates for physicians Vs general population. More revealing

are the reasons why they underwent CD. Lack of confidence in vaginal delivery due to the absence of electronic fetal monitoring, and fear of labor pain are the main reason why women choose elective CD. Rate of CD may be decreased by winning the confidence of the parturient mothers or their partners through instituting appropriate intrapartum fetal monitoring and labor analgesia protocols. Additionally, obstetricians and gynecologists should be keen to offer scientific information to patients emphasizing on maternal and neonatal risks of medically unjustifiable CDs. The high rate of repeat CD for history of one prior CD and other non-medical indications like maternal request and isolated oligohydramnios prompt the need to monitor appropriateness of these indications. It is important to note that CD is a major surgery with multiple complications and lack of evidence that CD brings benefit for low-risk pregnancies. Thus, it should be reserved only when there is a perceived risk which is an impediment to the life of the mother and/or the baby which can be offset with the application of CD.

DECLARATIONS

Availability of data and materials

The datasets used for this research are all included within the main text.

Abrevations

1. **ACSH** - Ayder Comprehensive Specialized Hospital
2. **CD** – Cesarean delivery
3. **CDMR** – Cesarean delivery for maternal request
4. **LMIC** – Low- and middle-income countries
5. TOLAC – Trial of labor after cesarean delivery

Acknowledgement

The authors would like to sincerely acknowledge physicians at Ayder Comprehensvie Specialized Hosptial for their willingness to participate in the study.

Funding

The authors did not solicit fund for this study.

Authors' Contributions

HT: Conceived research idea, designed the research, supervised, designed questionnaire, analyzed the data, drafted and reviewed the manuscript AY: Co-supervised, designed questionnaire, analyzed data, reviewed the manuscript. SA: Designed the research, designed questionnaire, analyzed data, reviewed the manuscript. MG, EB, HEA, AH, and EA: Participated in data analysis, reviewed the manuscript. All authors have read and approved the manuscript.

Declaration of Conflicting Interests

The authors have declared that no competeing interst exists.

CORRESPONDING AUTHOR:

Hale Teka, MD, OBGYN

Mekelle University, College of Health Sciences, Ayder Comprehensive Specialized Hospital, Tigray, Ethiopia

E-mail: haleteka@gmail.com

REFERENCES

1. Antoine, Clarel and Young, Bruce K. "Cesarean section one hundred years 1920–2020: the Good, the Bad and the Ugly" Journal of Perinatal Medicine, vol. 49, no. 1, 2021, pp. 5-16. https://doi.org/10.1515/jpm-2020-0305
2. Betran AP, Ye J, Moller A-B, et al. Trends and projections of caesarean section rates: global and regional estimates. BMJ Global Health 2021;6:e005671. doi:10.1136/ bmjgh-2021-005671
3. World Health Organization. Caesarean section rates continue to rise, amid growing inequalities in access [Internet]. Who.int. 2022 [cited 12 January 2022]. Available from: https://www.who.int/news/item/16-06-2021-caesarean-section-rates-continue-to-rise-amid-growing-inequalities-in- access
4. Beyene MG, Zemedu TG, Gebregiorgis AH, Ruano AL, Bailey PE. Cesarean delivery rates, hospital readiness and quality of clinical management in Ethiopia: national results from two cross-sectional emergency obstetric and newborn care assessments. BMC Pregnancy Childbirth. 2021;21(1):571. Published 2021 Aug 19. doi:10.1186/s12884-021-04008-9
5. Boatin A A, Schlotheuber A, Betran A P, Moller A, Barros A J D, Boerma T et al. Within country inequalities in caesarean section rates: observational study of 72 low and middle income countries BMJ 2018; 360 :k55 doi:10.1136/bmj.k55
6. Tadevosyan, M., Ghazaryan, A., Harutyunyan, A. et al. Factors contributing to rapidly increasing rates of cesarean section in Armenia: a partially mixed concurrent quantitative-qualitative equal status study. BMC Pregnancy Childbirth 19, 2 (2019). https://doi.org/10.1186/s12884-018-2158-6
7. ACOG Committee Opinion No. 761 Summary: Cesarean Delivery on Maternal Request, Obstetrics & Gynecology: January 2019 - Volume 133 - Issue 1 - p 226-227 doi: 10.1097/AOG.0000000000003007
8. Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: Systematic review and meta-analysis. PLoS Med. 2018;15(1):e1002494. Published 2018 Jan 23. doi:10.1371/journal.pmed.1002494
9. Tihtonen K, Nyberg R. Kohdun keisarileikkausarven pitkäaikais- vaikutukset [Long-term effects of uterine cesarean section scar]. Duodecim. 2014;130(5):461-8. Finnish. PMID: 24730196.
10. Astrid M. Otkjær,Henrik L. Jørgensen,Tine D. Clausen,Lone Krebs. Maternal short-term complications after planned cesarean delivery without medical indication: A registry-based study. AOGS. 30 January 2019; https://doi.org/10.1111/aogs.13549
11. ACOG. Safe Prevention of the Primary Cesarean Delivery: Obstetric Care Consensus No. 1. 2016;(3):1–19.
12. Solheim KN, Esakoff TF, Little SE, Cheng YW, Sparks TN, Caughey AB. The effect of cesarean delivery rates on the future incidence of placenta previa, placenta accreta, and maternal mortality. J Matern Fetal Neonatal Med. 2011 Nov;24(11):1341-6. doi: 10.3109/14767058.2011.553695. Epub 2011 Mar 7. PMID: 21381881.
13. Johnson, Erin M., and M. Marit Rehavi. 2016. "Physicians Treating Physicians: Information and Incentives in Childbirth." American Economic Journal: Economic Policy, 8 (1): 115-41.DOI: 10.1257/pol.20140160
14. Bihler J, Tunn R, Reisenauer C, Kolenic GE, Pauluschke-Froehlich J, Wagner P, Abele H, Rall KK, Naumann G, Wallwiener S, Wallwiener M, Sohn C, Brucker SY, Huebner M. The preferred mode of delivery of medical professionals and non-medical professional mothers-to-be and the impact of additional information on their decision: an online questionnaire cohort study. Arch Gynecol Obstet. 2019 Feb;299(2):371-384. doi: 10.1007/s00404-018-4970-7. Epub 2018 Nov 22. PMID: 30467635.
15. Hailegebreal, S., Gilano, G., Seboka, B.T. et al. Prevalence and associated factors of caesarian section in Ethiopia: a multilevel analysis of the 2019 Ethiopia Mini Demographic Health Survey. BMC Pregnancy Childbirth 21, 798 (2021). https://doi.org/10.1186/s12884-021-04266-7
16. Fesseha N, Getachew A, Hiluf M, Gebrehiwot Y, Bailey P. A national review of cesarean delivery in Ethiopia. Int J Gynaecol Obstet. 2011 Oct;115(1):106-11. doi: 10.1016/j.ijgo.2011.07.011. Epub 2011 Aug 26. PMID: 21872239.
17. Tadesse, H., Gessessew, A., & Medhanyie, A.A. trends and outcomes of cesarean delivery in Ayder comprehensive specialized hospital, Mekelle City, Northern Ethiopia. East Afr J Health Sci. 2019; 1(1).
18. Hemminki E, Klemetti R, Gissler M. Cesarean section rates among health professionals in Finland, 1990–2006. Acta Obstetricia et Gynecologica Scandinavica. 2009;88(10):1138-1144.
19. Gedefaw, G., Demis, A., Alemnew, B. et al. Prevalence, indications, and outcomes of caesarean section deliveries in Ethiopia: a systematic review and meta-analysis. Patient Saf Surg 14, 11 (2020). https://doi.org/10.1186/s13037-020-00236-8
20. Ruibin Deng, Xian Tang, Jiaxiu Liu, Yuwen Gao, and Xiaoni Zhong. Cesarean delivery on maternal request and its influencing factors in Chongqing, China. BMC Pregnancy and Childbirth. 2021; 21(384). https://doi.org/10.1186/s12884-021-03866-7

21. Yanfang Guo, Malia S Q Murphy , Erica Erwin, Romina Fakhraei, Daniel J Corsi, Ruth Rennicks White, Alysha L J Harvey, Laura M Gaudet, Mark C Walker , Shi Wu Wen, Darine El-Chaâr . Birth outcomes following cesarean delivery on maternal request: a population-based cohort study. CMAJ. 2021;193(18):E634-E644. doi:10.1503/cmaj.202262
22. American College of Obstetricians and Gynecologists. Committee on obstetric Prqctice. Cesarean delivery on maternal request. ACOG Committee opinion no. 761. Obstet Gynecol. 2019;133(1):e73–7. https://doi.org/10.1097/aog.0000000000003006.
23. Margo S. Harrison, Ana Garcesb, Lester Figueroab, Fabian Esamaic, Sherri Bucherd, Carl Bosee, Shivaprasad Goudarf, Richard Dermang, Archana Patelh, Patricia L. Hibberdi , Elwyn Chombaj , Miusaku Mwenechanyaj , Michael Hambidgea and Nancy F. Krebsa. Caesarean birth by maternal request: a poorly understood phenomenon in low- and middle-income countries. International Health 2021; 13: 63–69. doi:10.1093/inthealth/ihaa020
24. Mariyappa Narayanaswamy, Balagurusamy Ambikaa, Talasila Sruthia. Cesarean Delivery at Maternal Request in a Rural Medical College Hospital. J Clin Gynecol Obstet. 2016;5(2):64-67. doi: http://dx.doi.org/10.14740/jcgo290w
25. Yajuan Zhao, Shuangyun Chen. Psychosocial Factors for Women Requesting Cesarean Section. International Journal of Clinical Medicine, 2013, 4, 395-399. http://dx.doi.org/10.4236/ijcm.2013.49071
26. WHO Human Reproduction Programme. WHO statement on caesarean section rates. World Health Organization, GenevaApril, 2015. http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/cs-statement/en/
27. Sandall J, Tribe RM, Avery L et al.Short-term and long-term effects of caesarean section on the health of women and children. Lancet. 2018; http://dx.doi.org/10.1016/S0140-6736(18)31930-5
28. Burcher P. (2022) The Changing Ethical Landscape of Cesarean Delivery on Maternal Request. In: Lonchyna V.A., Kelley P., Angelos P. (eds) Difficult Decisions in Surgical Ethics. Difficult Decisions in Surgery: An Evidence-Based Approach. Springer, Cham. https://doi.org/10.1007/978-3-030-84625-1_23
29. Society of Obstetricians and Gynaecologists of Canada, the Association of Women's Health, Obstetric and Neonatal Nurses of Canada, the Canadian Association of Midwives, the College of Family Physicians of Canada, the Society of Rural Physicians of Canada. Joint policy statement on normal childbirth. SOGC Clinical Practice Guideline No. 221, December 2008. J Obstet Gynaecol Can 2008; 30:1163–5. Available at: http://www.sogc.org/ guidelines/documents/gui197CPG0709.pdf.
30. FIGO Ethics and Professionalism Guideline: Decision Making about Vaginal and Caesarean Delivery | Figo [Internet]. Figo. 2022 [cited 11 January 2022]. Available from: https://www.figo.org/decision-making-about-vaginal-and-caesarean-delivery
31. Ahmad H, Munim S. Isolated oligohydramnios is not an indicator for adverse perinatal outcome. J Pak Med Assoc. 2009 Oct;59(10):691-4. PMID: 19813684
32. Morris RK, Meller CH, Tamblyn J, Malin GM, Riley RD, Kilby MD, Robson SC, Khan KS. Association and prediction of amniotic fluid measurements for adverse pregnancy outcome: systematic review and meta-analysis. BJOG. 2014 May;121(6):686-99. doi: 10.1111/1471-0528.12589. Epub 2014 Feb 7. PMID: 24738894.

PREVALENCE OF EPISIOTOMY AND FACTORS ASSOCIATED WITH ITS PRACTICE IN THREE TEACHING HOSPITALS, ADDIS ABABA, ETHIOPIA

Eskinder Kebede[1], Yitbarek Fantahun, Sofia Hassen

ABSTRACT

BACKGROUND: Episiotomy is a surgical incision into the perineum and posterior vaginal wall during the second stage of labor to increase the diameter of the soft tissue pelvic outlet to facilitate delivery. Episiotomy rates vary from population to population. Limited information exists related to the practice of episiotomy in Ethiopia.

OBJECTIVE: To assess the prevalence of episiotomy practice and associated factors at three teaching hospitals (Tikur Anbessa Hospital, Gandhi Memorial Hospital, and Zewditu Memorial Hospital) in Addis Ababa Ethiopia.

METHOD AND MATERIALS: Hospital-based cross-sectional study was conducted from January 2022 to March 2022 on 386 mothers who had a vaginal delivery in the three hospitals. A structured questionnaire was used to collect data. The data was entered, coded, and analyzed using Statistical Package for Social Science (SPSS) version 25. Binary and multivariable logistic regression analyses were performed. P value ≤ 0.05 was used to determine the level of statistically significant variables.

RESULTS: The prevalence of episiotomy was 49%. Age ≤24 years (AOR=0.17, 95%CI=0.055, 0.52), duration of second stage of labor ≥2HR (AOR=3.5, 95%CI=1.87, 11.06), birth weight of newborn ≥4000 grams (AOR=5.3, 95%CI=95%CI, 1.28, 22.02) and FGM (AOR=2.8, 95%CI=1.64, 4.94) were factors significantly associated with episiotomy practice.

CONCLUSION: The prevalence of episiotomy in this study (49%) is higher than the WHO's recommendation (10%). Variables that remained associated significantly with episiotomy were maternal age, duration of the second stage of labor ≥2HR, newborn weighing ≥4000 grams, and FGM. An effort should be made to reduce the prevalence of episiotomy by giving emphasis on the restrictive use and adhering to the correct indications.

KEY WORDS: Episiotomy, prevalence of episiotomy, factors associated with episiotomy

(The Ethiopian Journal of Reproductive Health; 2023; 15;47-58)

1 Department of Obstetricians and Gynecologists, School of Medicine, Addis Ababa University, Addis Ababa, Ethiopia

INTRODUCTION

Episiotomy is a surgical incision into the perineum and posterior vaginal wall during second stage of labour to increase the diameter of the soft tissue pelvic outlet and to facilitate delivery[1]. The rate of episiotomy varied considerably from country to country around the world that range from 9.7% (Sweden) to 100% (Taiwan). It is important to highlight that, as any surgical procedure, episiotomy is also responsible for complications, such as perineum lesion extension, hemorrhage, edema, infection, hematoma, dyspareunia, rectovaginal fistulas, myonecrosis, neonatal intoxication from lydocaine, hypersensitivity reactions to anesthetics, endometriosis in the scar, need of surgical correction due to irregular or excessive cicatrization problems, pain after delivery or maternal rejection of the newborn due to pain[2].

It is first reported back in 1741 and continues to become part of modern obstetrics[3]. Routine use of episiotomy originally began by Pomeroy in 1918 & this routine practice was accepted and taught in obstetrics services till 1970s[1]. A routine use of episiotomy was proposed to prevent severe spontaneous perineal lacerations (third and fourth-degrees) by enlarging the vaginal outlet to reduce vaginal soft tissue stretching and tension during childbirth[1]. However, routine use of episiotomy has been questioned, because of its own related complications and the possibility to cause unnecessary trauma[2]. Since then many studies, reviews and met analyses have evidenced that there is no scientific basis for maintaining the routine practice of episiotomy. Restrictive episiotomy policies appear to have a number of benefits compared to policies based on routine episiotomy there is less posterior perineal trauma, less suturing and fewer complications, and although it has been associated with more anterior perineal trauma this type of trauma is not usually clinically significant[3-5]. Lacerations classified as first or second degree appear to be more advantageous than performing routine episiotomies as they are reported to heal better and result in less bleeding and less pain for the woman[6].

Although there is a global trend for reduced episiotomy rates, there is no universally accepted rate of episiotomy for non-operative vaginal delivery in a normal labor ward, but the world health organization recommends a rate of 10%, based on a 1984 English trial[8,9]. Despite current recommendations against routine use of episiotomy, its incidence continue to be very high in some center and areas of the world, with rates up to 60% and 80% in India and china, respectively[7].

In Ethiopia limited information exists related to the practice of episiotomy. Therefore, this study aimed to assess the prevalence of episiotomy and factors associated with its practice in three hospitals (TASH, ZMH & GMH) found in Addis Ababa, Ethiopia, which gives insight regarding the current practice. Knowing the current prevalence of episiotomy and its associated factor in Addis Ababa will help us to give recommendation on the rate of episiotomy which results in reduction of morbidity associated with it therefore; this study has been designed to fill the research gap. The objective of the study is to assess the prevalence of episiotomy and associated factors with its practice at three teaching hospitals in Addis Ababa Ethiopia.

METHOD

There are more than 12 public and more than 25 private hospitals in Addis Ababa city[11]. Of the total 12 public hospitals, 3 were selected by convenience. The study was conducted in three hospitals: Tikur Anbessa Specialized Hospital, Gandhi Memorial Hospital and Zewditu Memorial Hospital which are found in Addis Ababa, Ethiopia. These hospitals serve as central referral teaching hospitals and all obstetric emergencies including high risk pregnancies are referred to these hospitals from Addis Ababa and its vicinity.

Hospital based cross-sectional study design was used to assess the prevalence of episiotomy and factor associated with its practice at three hospitals found in Addis Ababa City Administration

The sample size of 386 determined using single population proportion formula by assuming 95% confidence interval, 5% margin of error and proportion the prevalence of episiotomy practice was 35.4% from the previous study was taken from a similar study done in Ethiopia[12]

Inclusion and Exclusion Criteria

Inclusion criteria

- Women who delivered vaginally at the three teaching hospital in the study period

Exclusion criteria

- Women who was critical after delivery
- Women who didn't give consent
- Women who delivered by distractive delivery

Data was collected by a pre-tested structured questionnaire developed by the investigator. Systematic random sampling technique was used to select study participants among mother who gave birth vaginally. The first study participant was selected by lottery method from those mothers who delivered by vagina: Then the next participant was identified systematically every other interval until the required sample size was achieved. After one hour of delivery after consent obtained from the mother, data was collected by the birth attendant through face to face interview using structured questionnaire and reviewing maternal records and checked for completeness by supervisor on the same day.

Data entry, cleaning and analysis was performed using SPSS version 25. Summary tables were used for describing data. A relationship among the major variables were described by significant level $P<0.05$. Logistic regression (using $P<0.05$) was used to examine the relationship between the proposed dependent and independent variables. For each regression odds ratios (with the accompanying p-values and confidence intervals) of the relationship was reported.

Operational Definitions

- Episiotomy is a surgical incision into the perineum and posterior vaginal wall during second stage of labour to increase the diameter of the soft tissue pelvic outlet and to facilitate delivery[13]
- Liquor status
  - Clear
  - Bloody
  - Meconium
- Fetal heart rate
  - Normal (120-160)
  - Bradycardia (<120)
  - Tachycardia (>160)
- Female genital mutilation comprises all procedures that involve partial or total removal of the external female genitalia, or other injury to the female genital organs for nonmedical reasons.

ETHICAL CLEARANCE

The proposal was approved by the Research and Publication Committee of Department of Obstetrics and Gynecology, Addis Ababa University. Informed oral consent was obtained from each participant before the start of data collection. To ensure confidentially of respondents, their names were not indicated on the questionnaire and it was assured that their responses will be kept strictly confidential. The anonymity and confidentiality of the participants was kept private. The name of the participants was not included in the data collection format.

RESULT

During the study period 386 mothers who gave birth vaginally were interviewed with the response rate of 100%. Half of the respondents were in the age group of 25-30 years. The average mean age of the respondents was 27.2±4.74 years. Majority of respondents were from urban area (95.6%) and sixty-one percent were housewives. Related to the educational status of the respondents 167 (43.3%) of them attended primary school and 102 (26.4%) were government employees.

Table 1. sociodemographic characteristics of mothers who gave birth vaginally at three teaching hospitals of Addis Ababa university, Addis Ababa, Ethiopia, 2022 (N-386)

Variable		Frequency	Percent
Age of the study participant			
	≤24	117	30.3
	25-30	195	50.5
	31-34	32	8.3
	≥35	42	10.9
Place residence			
	Urban	369	95.6
	Rural	17	4.4
Maternal occupation			
	Housewife	236	61.1
	Employee	102	26.4
	Merchant	34	8.8
	Student	9	2.3
	Other	5	1.3
Education status			
	No formal education	44	11.4
	Primary	167	43.3
	Secondary	95	24.6
	College and above	80	20.7

Fifty-eight percent of the respondents were multiparous and 235 (60.9%) had previous vaginal delivery. Among these mothers 175 (74.5%) of them had a history of previous episiotomy. forty-six percent had female genital mutilation and fifty-nine percent of the respondents were found to have a normal body mass index. In 10.4% of mothers, a previous history of chronic illness was reported (Table 2).

Table 2. obstetric characteristics of mothers who gave birth vaginally at three teaching hospitals of Addis Ababa university, Addis Ababa, Ethiopia, 2022 (N-386)

Variable		Frequency	Percent
Parity			
	Prim parous	139	36.0
	multiparous	223	57.8
	Grand multiparous	24	6.2
Previous vaginal delivery			
	yes	235	60.9
	no	151	39.1
History of previous episiotomy			
	yes	175	74.5
	no	60	25.5
Female genital mutilation			
	yes	179	46.4
	no	207	53.6
history of chronic illness specifies			
	cardiac	5	1.3
	chronic HTN	3	.8
	DM	7	1.8
	Asthma	1	.3
	others	24	6.2
	no	346	89.6
Body mass index			
	<=18.4	4	1.0
	18.5-24.9	230	59.6
	25-29.9	127	32.9
	>=30	25	6.5

Out of the 386 deliveries, in 75.6% of the cases labor started spontaneously, 97.9% of the respondent had singleton pregnancy, regarding gestational age of current pregnancy, 83.9 % were term, and 90.9% had normal fetal heart beat pattern in second stage. About 52.3% of respondents had given birth at night; sixty-three percent were delivered in less than one hours of second stage of labor; and 39.6% of deliveries were attended by midwives (Table3).

Table 3. The labor and delivery characteristics of mothers who gave birth vaginally at three teaching hospitals of Addis Ababa university, Addis Ababa, Ethiopia, 2022 (N-386)

Variable		Frequency	Percent
Types of pregnancy			
	Singleton	378	97.9
	Twin	8	2.1
Onset of labor			
	Spontaneous	292	75.6
	Induced	94	24.4
Use of oxytocin			
	Yes	168	43.5
	No	218	56.5
Condition of fetal heart rate during 2nd stage			
	Normal range	351	90.9
	Bradycardia	22	5.7
	Tachycardia	7	1.8
	Negative	6	1.6
Fetal presentation			
	Vertex	377	97.7
	Breech	6	1.6
	Face	3	.8
Shift of delivery completion			
	Night	202	52.3
	Day	184	47.7
Duration of Second stage of labor			
	≤1HR	245	63.5
	1-2HR	93	24.1
	≥2HR	48	12.4
Birth attendant			
	Midwife	153	39.6
	Resident	134	34.7
	Intern	99	25.6

According to this study the prevalence of episiotomy was found to be 49%. And the main reasons for performing episiotomy procedure were; anticipation of spontaneous perineal tears in 38.9% of the cases followed by soft tissue dystocia in 37.9% of cases. The episiotomy type was Medio-lateral in all the cases. Twelve percent of mothers who had episiotomy in the current pregnancy developed extension as a complication.

Among those who had no episiotomy in the current pregnancy, 21.9% of them develop first degree perineal laceration and 8.2 % of them developed Second degree perineal laceration. There was no third and fourth degree perineal laceration (Table 4).

Table 4 episiotomy related characteristics of mothers who gave birth vaginally at three teaching hospitals of Addis Ababa university, Addis Ababa, Ethiopia, 2022 (N-386)

Variable		Frequency	Percent
Types of episiotomies			
	Medio-lateral	190	100
Complications after episiotomy			
	no complication	123	64.7
	extension	24	12.6
	perineal hematoma	3	1.6
	PPH	8	4.2
	Perineal pain	32	16.9
For those who had no episiotomy is there perineal injury	No perineal injury	137	69.9
	First degree perineal injury	43	21.9
	Second degree perineal injury	16	8.2

Out of the total deliveries, 90.4% of fetus had clear liquor during second stage of labor. The birth weight of most of the babies delivered (81.3%) ranged from 2.5 Kg to 3.99 Kg and 12.7% had birth weight of ≥ 4 Kg, 94.3% and 98.2% of the newborns had an Apgar score of greater than 7 at 1st and 5th minutes respectively (Table 5).

Table 5 perinatal characteristics of mothers who gave birth vaginally at three teaching hospitals of Addis Ababa university, Addis Ababa, Ethiopia, 2022 (N-386)

Variable		Frequency	Percent
Gestational age during delivery			
	Preterm (<37wk	27	7.0
	Term (37-41+6)	324	83.9
	Post term (>=42wk	35	9.1
Status of liquor during second stage of labor			
	Clear	349	90.4
	Bloody	16	4.1
	Meconium	21	5.4
Newborn weight			
	≤2499	23	6.0
	2500-3999	314	81.3
	≥4000	49	12.7
APGAR score at one minute			
	0	6	1.6
	1-6	16	4.1
	≥7	364	94.3
APGAR score at five minutes			
	0	6	1.6
	1-6	1	.3
	≥7	379	98.2

The study showed that age of the mother, education status of the mother, parity, duration of second stage, scope of birth attendant, weight of the newborn and FGM are associated with episiotomy practice in bivariate analysis. But, after adjusting for possible confounder, only age of the mother, parity, duration second stage, weight of the newborn and FGM remain significantly associated.

Thus, multivariate analysis of this study revealed that participants whose age is ≥ 35 years are 83% less likely to have episiotomy than participant whose age is ≤ 24 years (AOR=0.17, 95%CI=0.055, 0.52) and Primigravidas were 5 times more likely to have episiotomy as compared to multigravidas (AOR=5.4,95%CI:1.23,7.42).

Duration of second stage of labor was another statistically significant variable. Duration of second stage of labor ≥2hr increase likelihood of having episiotomy by 3.4 folds than second stage of labor duration <1hr (AOR=3.5, 95%CI=1.87, 11.06). Women who delivered 4000 grams and above neonate had increased episiotomy rate by 5.3 folds (AOR=5.3, 95%CI=95%CI, 1.28, 22.02) and participant who had FGM increase the rate of episiotomy by 2.8 folds (AOR=2.8, 95%CI=1.64, 4.94) (Table 6).

Table 6. The bivariate and multivariate binary regression of independent variable with Episiotomy among study participants who gave birth vaginally in three teaching hospitals of Addis Ababa university, Addis Ababa, Ethiopia, 2022 (N-386)

Variable	Episiotomy		p-value	COR (95%CI)	P-value	AOR (95%CI)
	Yes	No				
Age of the study participant						
≤24	82	35	1		1	
25-30	89	106	0.000	0.36(0.22, 0.58)	0.012	0.46(0.26, 0.84)
31-34	13	19	0.003	0.29(0.13, 0.66)	0.179	0.50(0.18, 1.37)
≥35	6	36	0.000	0.07(0.03, 0.18)	0.002	0.17(0 .055, 0.52)
Education status						
no formal education	16	28	1		1	
primary	77	90	0.248	1.5(0.75, 2.97)	0.309	1.5(0.67, 3.48)
secondary	58	37	0.008	2.7(1.31, 5.75)	0.074	2.2(0.92, 5.44)
college and above	39	41	0.186	1.7(0.78, 3.54)	0.216	1.8(0.71, 4.48)
Duration of second stage						
≤1HR	99	146	1		1	
1-2HR	50	43	0.028	1.7(1.06, 2.77)	0.429	1.3(0.71, 2.24)
≥2HR	41	7	0.000	8.6(3.73, 20.03)	0.043	3.4(1.98, 11.45)
Birth attendant						
midwife	66	87	1		1	
resident	66	68	0.300	1.3(0.80, 2.04)	0.322	1.4(0.75, 2.44)
intern	58	41	0.017	1.9(1.12, 3.11)	0.372	0.73(0.36, 1.47)
Newborn weight						
≤2499	6	17	1		1	
2500-3999	148	166	0.058	2.5(0.97, 6.58)	0.096	2.6(0.85, 7.95)
≥4000	36	13	0.000	7.8(2.54, 24.19)	0.021	5.3(1.28, 22.02)
Parity						
primiparous	106	33	1		1	
Multiparous	80	143	0.000	0.17(0.11, 0.28)	0.310	0.47(0.11, 2.010
Grand multiparous	4	20	0.000	0.06(0.02, 0.19)	0.096	0.18(0.023, 1.35)
History of vaginal delivery						
yes	77	158	0.000	0.18(0.11, 0.29)	0.237	0.44(0.11, 1.71)
no	113	38	1		1	
Female genital mutation						
yes	104	75	0.001	1.95(1.30, 2.93)	0.000	2.8(1.64,4.94)
no	86	121	1		1	

DISCUSSION

This study revealed that the prevalence of episiotomy is 49% (95%CI=44.0, 54.0), quite high when it is compared to the world health organization recommendation which is 10%[9]. This study result is also higher when it is compared with the study conducted in Integrated Health Center at a Maternity School in Recife, Pernambuco, Brazil (29.1%), Public health institutions at Shire Town, in Ethiopia (35%) and in Akaki Kality, sub city of Addis Ababa, Ethiopia (35.2%) [2,10,12]

Whereas, the finding of this study is in line with studies conducted in Gondar city, North west Ethiopia which is 47.7%[14]. In contrast, this study has a lower prevalence of episiotomy compared to a study done in Romania (79.2%), Arba Minch General Hospital (68.0%) and Saint Paul's Hospital Millennium Medical College in Addis Ababa, Ethiopia (65.4%)[3,13,15].

This difference in the prevalence of episiotomy might be due to the difference in characteristics of the study population (low risk and high risk); the difference in time in which the study is conducted; and study settings (primary and referral centers).

The high prevalence of episiotomy in this study may be due to the characteristics of the study participants. That is, the three Hospitals (TASH, ZMH, and GMH) are referral hospitals, so most women who attend labor in these hospitals are high-risk mothers.

Among factors influencing the practice of episiotomy, this study showed participants whose age ≥35 years had 83% of less likely to have episiotomy than participant whose age ≤24 years (AOR=0.17, 95%CI=0.055, 0.52). Similar association was found with the study done in Brazil[2]

This may be due to the fact that, as age increase, the number of deliveries may increase, and multi parity have a significant effect on reduction of episiotomy rate, as also evidenced by the study done at Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia in which primigravidas were three times more likely to have episiotomy as compared to multigravidas (AOR=3.14,95%CI:1.058,9.357)[15].

In this study, duration of second stage labor greater than 2 hours increase episiotomy rate by 3.4 times as compared to those with less than 1-hour duration. This finding was similar with the study done in Saint Paul's Hospital Millennium Medical College Addis Ababa, Ethiopia and Bahirdar city, in Ethiopia[15,16].

The possible explanation might be due to increased need of intervention for prolonged second stage labor in order to reduce obstetric complications.

This study also showed that those mothers who gave birth to babies weighing more than 4000gm were 5.3 times more likely to have episiotomy. Similar association was found in the studies done in Brazil, Akaki Kality, sub city of Addis Ababa, Ethiopia and Saint Paul's Hospital Millennium Medical College Addis Ababa, Ethiopia[2,10,15]. This might be due to the need to have adequate space for higher fetal weight in order to prevent perineal laceration.

Another statistically significant factor for episiotomy was the history of female genital mutilation in participants. That is, FGM increases the likelihood of episiotomy by 2.8 folds. This may be the result of the need to release the tight perineum resulting from scar tissue formed after FGM, as it won't stretch during second stage labor

CONCLUSION

In this study the prevalence of episiotomy was 49% (95%CI=44.0, 54.0) which is significantly high when compared with the WHO's recommendation (10%) (9). Variables that remained associated significantly with increased rate of episiotomy were primigravidity, duration of second stage of labor ≥ 2 hours, newborn weight ≥ 4000 grams and FGM. Variable that remained associated significantly with decreased rate of episiotomy was maternal age ≥ 35. A maximum effort should be made to reduce the prevalence of episiotomy by giving emphasis on the restrictive use and by adhering to the correct indications. Different stakeholders working on maternal health programs should work on those factors associated with episiotomy and

create awareness regarding FGM related obstetric complication in order to reduce the prevalence of episiotomy. I recommend further study by using another study design to ascertain cause relationships.

DECLARATIONS

Limitations and Strength of this study

The cross-sectional nature of the study is not able to assess variables related to postoperative outcome because the cause and effect relationships could not be determined.

There may be bias since the data collector was birth attendant.

This study was conducted in three hospitals which makes it more representative.

Abbreviations

CI: Confidence Interval; CHS: College of Health sciences; FGM: Female Genital Mutilation; NGO: Nongovernmental Organization; SVD: Spontaneous Vaginal Delivery; TASH: Tikur Anbessa Specialized Hospital; ZMH: Zewditu Memorial Hospital; WHO: World Health Organization

Authors' contributions

SH designed and implemented the study. This included seeking DRPC approval, collecting data, and cleaning data. EK SH and YF reviewed the reference articles, performed data analysis, and wrote the initial manuscript. EK contributed wrote the final manuscript.

Competing interests; All authors declare that they have no competing interests.

CORRESPONDING AUTHOR:
Eskinder Kebede, MD
Department of Obstetricians and Gynecologists, School of Medicine, Addis Ababa University, Addis Ababa, Ethiopia
Email: eskinderkebede@yahoo.com

REFERENCES

1. Christophe Clesse JL-A, Sylvie De Lavergne, Sandrine Hamlin & Michèle Scheffle. Social-historical evolution of the episiotomy practice: A literature review. Women & Health. 2019:16.
2. Carvalho C, Souza A, Moraes Filho OB. Prevalence and factors associated with practice of episiotomy at a maternity school in Recife, Pernambuco, Brazil. Revista da Associacao Medica Brasileira (1992). 2010;56(3):333-9.
3. Fikadu KB, N. Tadesse, B. Mesele, D. Aschenaki, E. Toka, E. Arega, F. Girma, T. Paulos, A. Magnitude of Episiotomy and Associated Factors among Mothers Who Give Birth in Arba Minch General Hospital, Southern Ethiopia: Observation-Based Cross-Sectional Study. J Pregnancy. 2020;2020:8395142.
4. Franchi MP, Francesca Lazzari, Cecilia Garzon, Simone Laganà, Antonio Simone Raffaelli, Ricciarda Cromi, Antonella Ghezzi, Fabio. Selective use of episiotomy: what is the impact on perineal trauma? Results from a retrospective cohort study. Archives of gynecology and obstetrics. 2020;301(2):427-35.
5. Carroli G, & Mignini, L. . Episiotomy for vaginal birth. The Cochrane database of systematic reviews. 2009;(1), CD000081. https://doi.org/10.1002/14651858.CD000081.pub2.
6. Flora MB da Silva SMdO, Debra Bick, Ruth H Osava, Esteban F Tuesta and Maria LG Riesc. Risk factors for birth-related perineal trauma. Journal of Clinical Nursing. 2012(CLINICAL ISSUES):10.
7. Episiotomy Rates Around the World: An Update [Internet]. BIRTH 2005.
8. Variation in and factors associated with use of episiotomy [Internet]. JAMA. 2015 Jan 13.
9. OT Oladapo ÖT, M Bonet,TA Lawrie,A Portela,S Downe,AM Gülmezoglu. WHO model of intrapartum care for a positive childbirth experience: transforming care of women and babies for improved health and wellbeing. BJOG An international Journal of obstetrics and gynecologyJuly 2018. p. 8.
10. Worku SA MY, Getahun SA. Episiotomy Practice and its Associated Factor among Women Who Gave Birth at Public Health Institutions of Akaki Kality in Addis Ababa, Ethiopia. Clinics Mother Child Health. 2019;16:318. doi:10.24105/2090-7214.16.318.
11. Agency) CCS. Population Projection of Ethiopia for the Year 2014. Federal Democratic Republic of Ethiopia, Central Statistical Agency, Addis Ababa, . Scientific research. 2013;4-38.
12. Niguse KG, Gebreamlak Gebrehiwot, Haftom Abay, Mebrahtu Getachew, Darie Worku, Temesgen. Episiotomy Practice and its associated factors among mothers who gave birth vaginally at public health institutions of Shire Town, Northern Ethiopia. Infection. 2016;8:9.
13. Pasc A, Navolan D, Puscasiu L, Ionescu CA, Szasz FA, Carabineanu A, et al. A multicenter cross-sectional study of episiotomy practice in Romania. J Eval Clin Pract. 2019;25(2):306-11.
14. Teshome YM, Mengistu Sisay, Tariku Chala, Getahun Mengistu, Amanuael Shewasinad, Sisay Worku, Negese. Prevalence of Episiotomy and Its Associated Factors in University of Gondar Comprehensive Specialized Referral Hospital: A Retrospective Study from Ethiopia. American Journal of Life Sciences. 2020;8(1):9.
15. Tefera TK, Birhanu Mekonen, Tadios. Prevalence of episiotomy and factors associated with Practice of episiotomy at Saint Paul's Hospital Millennium Medical College: a cross sectional study. Ethiopian Journal of Reproductive Health. 2019;11(3):8.
16. Beyene FN, A. A. Limenih, S. K. Tesfu, A. A. Wudineh, K. G. Factors Associated with Episiotomy Practices in Bahirdar City, Ethiopia: A Cross-Sectional Study. Risk Manag Healthc Policy. 2020;13:2281-9.
17. Gachon B, Fritel, X., Rivière, O. et al. French guidelines for restrictive episiotomy during instrumental delivery were not followed by an increase in obstetric anal sphincter injury. Sci Rep 2022;12, 6330 . https://doi.org/10.1038/s41598-022-10379-6.

A POSTPARTUM UTERINE DEHISCENCE IN A PREGNANT WOMAN WITH BRUCELLOSIS: A CASES REPORT

Monireh Mirzaie[1], Zahra Yazdi[1], Azadeh Asgarian[2], Marzieh Savari[1]

INTRODUCTION

Uterine Dehiscence (UD) is a rare complication and very dangerous complication of cesarean section (CS). Brucellosis is a threatening infection in pregnant women with severe obstetrics outcomes such as spontaneous abortion, premature delivery, intrauterine infection. We presented a case with preterm delivery with continuing high fever due to uterine fascial dehiscence after CS, who were infected to brucellosis.

CASE: A 26-year-old woman with gravidity 1, referred to the obstetrical department at 30 weeks of gestation due to Preterm Premature rupture of membranes (PPROM). After vaginally sonography, the patient underwent emergency CS due to fetus FHR drop and umbilical cord prolapse. From second day after CS, the patients fever increased and Doppler sonography shows low fluid and hematoma in the uterus and evidence in favor of a lesion collection that was evacuated with laparotomy and uterine fascial dehiscence was detected. Moreover, wound debridement conducted and during laparotomy the adhesions were released. The Wright-Coombs 2ME test showed she was infected to brucellosis.

CONCLUSION: Uterine fascia dehiscence in lower uterine segment incision is a rare but is a potentially dangerous for mothers. However, preterm deliveries due to PPROM and high uncontrolled fever after CS, are conditions that practitioners should considering the uterine dehiscence to their differential diagnoses. Nevertheless, the occurrence of dehiscence due to brucellosis infection is questionable and require more evaluation.

KEY WORDS: Uterine dehiscence, Fascia, Cesarean section, Brucellosis, Premature rupture

(The Ethiopian Journal of Reproductive Health; 2023; 15;59-63)

1 Department of Obstetrics and Gynecology, Clinical Research Development Unit, School of Medicine, Nekouei-Hedayati-Forghani Hospital, Qom University of Medical Sciences, Qom, Iran
2 Department of Nursing, Clinical Research Development Unit, Nekouei-Hedayati-Forghani Hospital, Qom University of Medical Sciences, Qom, Iran

INTRODUCTION

The incidence of cesarean section (CS) operation is increasing in all countries especially in developing countries as the most common in obstetrics surgery[1]. Due to the CS operation, late scar dehiscence may occur in some women and may lead to uterine rupture in future pregnancies[1, 2]. Partial or complete Uterine Dehiscence (UD) following endomyometritis (puerperal sepsis) is a rare complication of lower segment cesarean section (LSCS) delivery[3]. This rare occurrence is very dangerous and potentially life threatening complication of CS with limited literature[4, 5].

Preterm delivery, tertiary cesarean delivery or higher and short inter-delivery interval of lower 24 months are the most important cases of UD.[2] Moreover, heavy vaginal postpartum hemorrhage(PPH), abdominal pain and pelvic pain as early as 11 days to as late as 12 weeks after surgery are the most common symptoms of UD in other reported cases.[6, 7]

Brucellosis is a threatening infection in pregnant women with severe obstetrics outcomes such as spontaneous abortion, premature delivery, intrauterine infection[8-10] We experienced a case with continuing high fever due to uterine fascial dehiscence after preterm delivery by CS, three days after the operation without any PPH, but who were infected to brucellosis.

CAUSE HISTORY

The patient was a 26-year-old gravida 1 woman, referred to the obstetrical emergency department at 30 weeks of gestation due to Preterm Premature rupture of membranes (PPROM). She had no symptoms of dizziness, nausea, vomiting, fever, purulent discharge, edema, and foot varicose veins. She has no history of taking a specific drug or underlying disease, with a 4 years of infertility history, but the current pregnancy was automatic. She was satisfied from the fetus movements and she report consumption of local (unpasteurized) dairy.

In the first day, the vital signs after admission was BP:95/60, PR=92, RR=19 and T=36.5°. The clinical examination showed the abdomen is soft and without guarding. Lungs were normal and vesicular. She has not uterine tenderness and in uterine examination by speculum, the cervix was closed. The fetus FHR was 135. Therefore, after clinical examinations Ampicillin (AMP, 2gr; QID-IV, no discharge), Azithromycin (Cap, gr P.O, Stat), Betamethasone (AMP,12mg I.M Stat), Magnesium sulfate (2 gr, Stat for 12 hrs.) and NST +Toco (daily) was prescribed for patient.

During the fetal ultrasound on the first day of hospitalization a cephalic embryo, amniotic fluid= 132, and a posterior placenta was observed in uterine. The fetus weight was 1690 and was in 90th percentile of growth curve. The conducted biophysical was 10/10.

During the second and third days, the vital symptoms were stable and no fever was detected. In the second day after admission, in trans-vaginal sonography showed the length of the cervix was 23mm and the cervix path was open and qualified. In third day, due to FHR drop, fetal heart failure and umbilical cord prolapse, the patient underwent emergency cesarean section (CS). During CS, first the Pfannestiel incision conducted on abdomen and horizontal incision in lower segment of uterine applied. But due to back down transverse of fetus, the incision changed to T incision to achieve the fetus. The CS outcome was a fetus with PH=7.26, PCO2=50.1, PO2=15, HCO2=22.5, BE-CCF= -4.8, BE-B=-5.2, weight 1700gr and Apgar is first and 5 minutes was 7 and 9, respectively. Due to high risk of mother following cesarean, Ampicillin (2gr, QID), Gentamicin (80gr, TDS) and Clindamycin (900, TDS) prescribed for 48 hrs.

The first day after CS, the patient's general condition was good. The bandage site was dry and vaginal bleeding was normal and the uterus is contracted. Nevertheless, she has not defecation. On the second day after the CS, the patients had defecation, but at 11pm, her fever was 37.9 and she had tachycardia. On the third day after the CS, due to high fever, PCR Covid 19 and without contrast CT from

abdominal/pelvic was requested. Moreover, Apotel (Amp), Enoxaparin (Amp, 400mg BD), Pentazole (Tab, 20mg BD) is ordered.

In forth day after CS, infectious disease specialist replaced Vancomycin (AMP, 4.5 gr, QID) and Tasosin (AMP, 1 gr, BD) with Ampicillin (2gr, QID), Gentamicin (80gr, TDS) and Clindamycin (900, TDS). In addition, blood culture showed the proteinuria and PCR Covid-19 test were negative and the CXR did not show lung perfusion involvement. In forth day after CS, Doppler sonography did not show evidence of deep vein thrombosis (DVT) and pelvic artery thrombosis. Moreover, low fluid and hematoma in the uterus and evidence in favor of a subcutaneous lesion collection in 20 × 22 × 48 diameters was seen. The vital sign was BP:116/81, PR:130, RR:21, and T=39.3°. Moreover, CRP was higher 1200 and leukocytosis (WBS=12500) and neutrophil was 80%. Five days after CS, based on the medical commission, the patient was transferred to the operating room and subcutaneous lesion collection was evacuated with laparotomy. Uterine fascial dehiscence was not seen and a little post operation inflammation was seen at the site of CS. The culture of lesion collection showed positive E-Coli and therefore, Tasocin was hold but vancomycin, Meropenem (1gr, IV, TDS), Pantazol (Amp, 40mg) and Enoxaparin (40ml Daily) were prescribed.

After operation at fifth day and 10th days after CS all things was normal. On the 11th day after CS, a purulent discharge was observed during the washing of the wound and due to a 37.9 degrees' fever, the infection probability at the operation site or an abscess was raised. Therefore, a biopsy was then taken from the wound tissue for culture and Wright and Coombs 2ME test was requested. The patient, went to the operating room again due to high fever and for debridement of dehiscence. She underwent NPO in last night and transferred to the operating room by diagnosing infection of CS wall without purulent discharge. Laparotomy was performed and during laparotomy the dehiscence were released and then she was transferred to the ICU.

During washing and debridement in the operating room, we noticed fascia dehiscence, in which the fascia opened and we entered the abdominal cavity, and uterine dehiscence was completely seen in the T-incision. Debridement and repair of the uterus were performed and the uterus was preserved. Therefore, fascia and infection debrided and fascia was repaired, then drain was implanted and cutaneous and subcutaneous of skin maintained open. Then, two units of pack cells, 2 units of FFP and Apotel (Amp) and continuing vancomycin and Meropenem (1gr, IV, TDS) is prescribed.

On 15th day after CS, the wound site was dry and wound culture for negative Coagulase Staff of uterine fascia dehisce were negative. Vancomycin discharged and Linezolid started and Meropenem Continued. Laboratory results showed that Wright (1/1280) and Coombs 2ME (1/1280) tests was positive and brucellosis diagnosis confirmed. Therefore, the brucellosis treatment started with tetracycline orally (500 mg, every 6 hours for 8 weeks) and gentamicin (3-5 mg/kg for 2 weeks). Finally, at 19th day after CS, the patient discharged by continuing medication and antibiotic therapy and outpatient follow-up. Finally, resection of the uterine defect and re-constitution of the uterine wall was successfully achieved and brucellosis treated.

DISCUSSION:

Dehiscence of a cesarean scar incidence varied between 0.3–1.9% of all cases and uterine hemorrhage did not occurs in majority of cases[3,6,7]. Therefore, other symptoms such as infection in wound and dehiscence sites should be considered in evaluation of postpartum pain after CS. In addition, coinfection by brucellosis of other microbial agents should be considered in differential diagnosis. Other studies demonstrated that multiparty, infection, and an incision placed too low in the lower uterine segment are the risk factors for dehiscence in LSCS[3].

Infections and subsequent spillage of pathogenic organisms into the peritoneum are the cause of weakening in uterine scar tissue and occurred the peritonitis or abscess formation. Similar consequence observed in the myometrium during LSCS, which the gradual spread of intra-uterine pathological organisms into the peritoneal cavity is occurred and caused facial dehiscence[4,11]. Among diagnostic methods, 3D ultrasound is better method for detection of dehiscence than routine transvaginal ultrasound that is applicable for fluid collection or hematoma in the scar area[6].

The uterine culture in current case, did not show any microbial infection, but the wound culture was positive twice that E. coli in the first time and negative Coagulase Staff in second time. Therefore, she received a broad spectrum antibiotic cover to healing their wound and control her fever. However, due to long time fever, and history of unpasteurized dairy, premature delivery and intrauterine infection brucellosis tests were checked. However, other articles showed that delayed cesarean wound healing may be due to infection[7].

According to literatures multiparty, infection, and an incision placed too low in the lower uterine segment are related risk factors for dehiscence of the lower segment uterine scar following CS[3]. In current case, uterine fascia dehiscence may be related to brucellosis infection and the persistent fever despite adequate antimicrobial therapy was the cause of delayed wound healing. Nevertheless, in this case, due to antibiotics prophylaxis after CS, the sepsis did not occur, but the brucellosis infection may be the main cause of high fever and delayed healing. Brucellosis as a common and threatening infection in pregnant women could cause localized body system complications, osteoarticular system and severe obstetrics outcomes such as spontaneous abortion, premature delivery, intrauterine infection or intrauterine fetal death (IUFD) in pregnant women with brucellosis[8-10]. The same condition conducted in current patients and our cases pregnancy terminated at 29th week of gestational age. Nevertheless, the fetus was not infected to brucellosis and was normal.

In the presented cases the laparotomy conducted two times and in the first time the subcutaneous lesion collection was evacuated at 4th day after CS and another laparotomy operation was conducted at 11th day after CS and adhesions were released. Nevertheless, the uterine of our case was preserved, but the consequences of this complication is unknown for a future pregnancy.

Uterine scar separation should be executing in patients with a fascial dehiscence after CS delivery and patients should be counseled for hysterectomy at laparotomy time for especial situations.[12] Moreover, transvaginal sonography of the scar region is necessary in patients with CS history to screening the latent scar dehiscence in combination with uterine wall thinning before planning further pregnancy. In cases who were suspected to uterine dehiscence, combined laparoscopic - vaginal or vaginal sonography is useful for repair the defect.[1]

CONCLUSION:

Uterine fascia dehiscence in lower uterine segment incision is a rare but is a potentially dangerous for mothers. This outcome should be considered in patients with history of CS who were deciding for future pregnancy. However, preterm deliveries due to PPROM and high uncontrolled fever after CS, are conditions that practitioners should considering the uterine dehiscence to their differential diagnoses. Nevertheless, the occurrence of dehiscence due to brucellosis infection is questionable and require more evaluation.

CORRESPONDING AUTHOR:

Marzieh Savari, MD
Department of Obstetrics and Gynecology, School of Medicine, Nekouei-Hedayati-Forghani Hospital, Qom University of Medical Sciences, Qom, Iran,
Email: marzieh.savari@gmail.com

REFERENCES

1. Klemm P, Koehler C, Mangler M, Schneider U, Schneider A. Laparoscopic and vaginal repair of uterine scar dehiscence following cesarean section as detected by ultrasound. Journal of perinatal medicine. 2005;33(4):324-31. Epub 2005/10/07. doi: 10.1515/jpm.2005.058. PubMed PMID: 16207118.
2. Ramadan MK, Kassem S, Itani S, Sinno L, Hussein S, Chahin R, et al. Incidence and Risk Factors of Uterine Scar Dehiscence Identified at Elective Repeat Cesarean Delivery: A Case-Control Study2018.
3. Wagner MS, Bédard MJ. Postpartum uterine wound dehiscence: a case report. J Obstet Gynaecol Can. 2006;28(8):713-5. Epub 2006/10/07. doi: 10.1016/s1701-2163(16)32236-8. PubMed PMID: 17022911.
4. Haridas M, Tenneti VJD, Joshi A. Uterine Dehiscence: A Rare Cause of Postpartum Puerperal Sepsis. Cureus. 2021;13(9):e18264-e. doi: 10.7759/cureus.18264. PubMed PMID: 34722045.
5. Larsen JV, Janowski K, Krolilowski A. Secondary post partum haemorrhage due to uterine wound dehiscence. Cent Afr J Med. 1995;41(9):294-6. Epub 1995/09/01. PubMed PMID: 8591641.
6. Sengupta Dhar R, Misra R. Postpartum Uterine Wound Dehiscence Leading to Secondary PPH: Unusual Sequelae. Case reports in obstetrics and gynecology. 2012;2012:154685-. Epub 2012/06/07. doi: 10.1155/2012/154685. PubMed PMID: 22720176.
7. Baba T, Morishita M, Nagata M, Yamakawa Y, Mizunuma M. Delayed postpartum hemorrhage due to cesarean scar dehiscence. Arch Gynecol Obstet. 2005;272(1):82-3. Epub 2005/05/24. doi: 10.1007/s00404-004-0662-6. PubMed PMID: 15909191.
8. Liu Z, Wei D, Li Y, Zhou H, Huang D, Guan P. Different Clinical Manifestations of Human Brucellosis in Pregnant Women: A Systematic Scoping Review of 521 Cases from 10 Countries. Infection and drug resistance. 2020;13:1067-79. doi: 10.2147/IDR.S248779. PubMed PMID: 32341659.
9. Alsaif M, Dabelah K, Featherstone R, Robinson JL. Consequences of brucellosis infection during pregnancy: A systematic review of the literature. International Journal of Infectious Diseases. 2018;73:18-26. doi: https://doi.org/10.1016/j.ijid.2018.05.023.
10. Bosilkovski M, Arapović J, Keramat F. Human brucellosis in pregnancy - an overview. Bosnian journal of basic medical sciences. 2020;20(4):415-22. doi: 10.17305/bjbms.2019.4499. PubMed PMID: 31782698.
11. Sholapurkar SL. Etiology of Cesarean Uterine Scar Defect (Niche): Detailed Critical Analysis of Hypotheses and Prevention Strategies and Peritoneal Closure Debate. Journal of clinical medicine research. 2018;10(3):166-73. Epub 2018/01/26. doi: 10.14740/jocmr3271w. PubMed PMID: 29416572.
12. Treszezamsky AD, Feldman D, Sarabanchong VO. Concurrent postpartum uterine and abdominal wall dehiscence and Streptococcus anginosus infection. Obstetrics and gynecology. 2011;118(2 Pt 2):449-51. Epub 2011/07/20. doi: 10.1097/AOG.0b013e31821619e9. PubMed PMID: 21768850.

INSTRUCTION TO AUTHORS

1. Type of Articles

The Ethiopian Journal of Reproductive Health (EJRH) publishes original articles, review articles, short reports, program briefs, and commentaries on reproductive health issues in Ethiopia, and the African region. EJRH aims at creating a forum for the reproductive health community to disseminate best practices, and relevant information on reproductive health.

Original Articles: Articles reporting on original research using quantitative and/or qualitative studies could be submitted to EJRH.

Review Articles: Review articles on all aspects of reproductive health issues could be considered for publication in the EJRH.

Commentaries: Commentaries on any aspects of reproductive health in Ethiopia or the African region will be considered for publication in the EJRH.

Program Briefs: A one or two pages of description of a program run by governmental or non-governmental organizations could be submitted for publication. These briefs should give short summaries about the objectives, strategies for implementation, and expected outputs of programs that are executed by different organizations.

Short Reports: Preliminary research findings or interesting case studies could be presented in a summarized form to the journal.

2. Uniform Requirements

In order to fulfill uniform requirements for the journal, the following instructions have to be followed by authors: The manuscript should be a total of 3000 to 4000 words. Manuscript layout: Manuscripts should be written in English and typed double-spaced leaving generous margins. Pages should be consecutively numbered. The body of the manuscript should be organized under appropriate headings and sub-headings such as introduction, methods, results, discussion, acknowledgements, and references.

Title page: The title page should have title of the article; name of each author and institutional affiliation, and address of the corresponding author.

Abstracts: It should not be more than 250 words. It should summarize the background, objective, methods, major findings and conclusions.

Tables and Figures: All tables and figures should be submitted on separate sheets of paper and be clearly labeled in the order of their citation in the text. A reader should be able to read only the tables and easily understand all information without reading the text.
References: References have to be numbered consecutively in the order in which they are first mentioned in the text. References must also follow the Vancouver system.

EJRH

Visit us at www.ejrh.org

ISSN: 2520-0275 (Print)
ISSN: 2520-0283 (Online)